REMARKS

Claims 8, 9 and 16-23 are pending in this application. Claims 19-20 and 22-23 are withdrawn. Claims 1-7, and 10-15 are cancelled. Claims 8, 16, 17 and 18 are amended. Support for the amendments to these claims can be found, for example, in cancelled claim 1, and in the specification on page 5, lines 6-12. The amendments are being made to place the application in condition for allowance. Reconsideration is respectfully requested in view of the following remarks.

I. Revised Sequence Listing

Upon review of the instant application, Applicants note that the sequence listing submitted on September 12, 2001 included an error in the sequence for SEQ ID NOS: 1 and 2. The error consisted of inadvertently translated amino acids in the 5' end of the protein sequence. Applicants respectfully submit herewith a revised sequence listing for the Examiner's consideration.

II. Claim Rejection Under 35 U.S.C. 101

The Examiner rejected claims 8, 9, 16-18 and 21 under 35 U.S.C. § 101, as being allegedly not supported by either a credible asserted utility or a well established utility. Applicants respectfully traverse this rejection.

The Examiner states that the "state of the art in protein function prediction from amino acid sequence" is represented by Whisstock et al. (Q Rev. Biophys. 36:307-340 (2003)). The Examiner characterizes Whisstock's teachings as stating that: 1) protein function prediction is a difficult problem since homologous proteins often have different and multiple functions; 2) methods for inferring function based on similarity in sequence and/or structure between an unknown protein and one or more well-understood proteins is tenuous and only provide guesses at function; 3) protein function predictions suggest function but do not determine function; 4) the most useful effect of protein function prediction is to guide laboratory experimentation to confirm, refute or correct the prediction; and 5) protein function prediction from protein

sequence and structure is useful but is not a substitute for laboratory experimentation. See Office Action, pg. 3.

Firstly, Applicants respectfully point out to the Examiner that the Federal Circuit and the Patent Office guidelines have consistently rejected the use of a *per se* rule rejecting homology-based assertions of utility because such assertions are not based on relevant scientific evidence. Fed. Reg. 66:1096 (Jan. 5, 2001), citing *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995) (rejection of claims improper where claims did "not suggest an inherently unbelievable undertaking or involve implausible scientific principles" and where "prior art ... discloses structurally similar compounds to those claimed by the applicants which have been proven ... to be effective"). Instead, relevant precedent consistently supports a case-by-case analysis, taking into account "both the nature and degree of the homology." *Id.* The Federal Circuit has echoed this sentiment by establishing a broad presumption when an applicant asserts a claim for utility, as well as the lack of a need for absolute correlation when asserting function of a nucleic acid or protein sequence based on homology studies. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Id.*, citing *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565 (Fed. Cir. 1996).

Applicants here have asserted a specific and substantial utility for use of the protease-related protein ("PVP") in the regulation of keratinization of hair, which has utility in either hair loss or excess body hair therapeutic scenarios, by establishing a "reasonable correlation" using experimental data, as well as data available to one of ordinary skill in the art at the time of filing of the instant patent application. Applicants base this assertion partially on PVP's homology with respect to "a protease of the kallikrein family, optionally a protease activity." See Specification, pg. 2, lines 16-17. For clarification purposes, kallikrein proteins are a group of serine proteases that were first introduced in the 1930's. *See infra* Exhibit B. Although the actual sequence comparisons with various proteases and kallikrein protease proteins are not included with the specification, one of ordinary skill in the art could easily perform a protein sequence search, for example, through the publicly available and widely used National Center for Biotechnology Information protein-BLAST search engines to visualize the high degree of homology of PVP with proteases, including kallikreins, from various species. Applicants respectfully provide herewith for the Examiner's consideration, an example of results from a

BLAST search of the amino acid sequence of the claimed invention with protein sequences, demonstrating the significant structural relationships between PVP and proteases, including kallikrein proteins, that were known to one of ordinary skill in the art at the time of filing of the instant application. See Exhibit A, attached herein. The BLAST search found significant homology with several kallikrein and protease proteins, including: Kallikrein 6 [Rattus norvegius]; Kallikrein 8, isoform 2 [Homo sapiens]; Kallikrein 14 preproprotein [Homo sapiens]; KLK (kallikrein) 15 [Saguinus oedipus]; Kallikrein 11 isoform 2 precursor [Homo sapiens]; Serine protease [Rattus rattus]; Serine protease [Mus musculus]; and Trypsin precursor [Xenopus laevis].

Applicants assert, therefore, that even if the Whisstock reference is taken into account, the conclusion based on the BLAST search results can only be that significant homology is present between known kallikrein proteins and PVP, and that PVP's function can be reasonably correlated with that of a protease, including serine proteases of the kallikrein family. For example, Whisstock teaches that "the most favorable result is to find that the query sequence is identical or very closely related to that of a well-characterized protein." See Whisstock, pg. 321. In addition, Whisstock teaches that sequence similarity in regions of active site residues is also important in obtaining reliable functional predictability from homology comparisons. *Id.* at pg. 321-22. Whisstock concludes, "In general, if an unknown protein shares significant sequence similarity with a family of known function, possesses the 'right essential conserved residues' (e.g. active site residues) then a prediction as to function (proteinase, exonuclease, etc.) can reasonably be proposed." *Id.* at pg. 324.

Applicants assert that, as supported by Whisstock, the high degree of homology of greater than 50% with protease proteins, particularly with the well-characterized family kallikrein serine proteases, supports the function of PVP as a protease. Combined with the showing of homology across multiple species, from humans to monkeys to rats, the homology evidence points to the function of PVP as a member of a protease family. See Exhibit A. Moreover, the strong degree of homology within the active catalytic subunits of the protein, namely amongst histidine (WVLTAA**H**C), serine (GD**S**GGPL), and to a lesser extent, aspartic acid (**D**LMLL) motifs, only further supports the contention that PVP shares enzymatic protease function with the kallikrein protein family. See Yousef and Diamandis, Endocrine Rev. 22:184-

204 (2001) and active site comparisons, herein attached respectively as Exhibits B and C. As seen from Exhibit C, which compares kallikrein protein sequences with PVP and highlights active site residues for both kallikrein and PVP proteins, PVP shares extensive homology with rat, monkey and human kallikreins in the active site regions. Importantly, the active site residues characteristic for kallikrein proteins are highly conserved in PVP. Based on the homology and active site comparison data alone, Applicants have sufficiently shown, therefore, that PVP is related to a protease protein, lending support to their utility of PVP as a protease protein.

Moreover, Applicants have shown, in addition to the knowledge of one of ordinary skill in the art at the time of filing, important functional data in regards to PVP and hair growth regulation. One of ordinary skill in the art would know at the time of filing of the role that serine proteases play in keratinocyte regulation. For example, past studies have shown that serine proteases can induce apoptosis in keratinocyte cell lines, as well as in vivo in actively growing hair follicles. *See* Seiberg, M. et al., "Trypsin-induced follicular papilla apoptosis results in delayed hair growth and pigmentation," Dev. Dyn. 208: 553-564 (1997), Exhibit D, attached herein. Apoptosis, or programmed cell death, plays a large role in the active growth cycle of hair follicles in the catagen phase, where the hair follicle shortens as its lower two third of the follicle structure undergoes programmed cell death and apoptosis. *Id.* at pg. 553, col. 1, 1st paragraph. Treatment of mice with the serine protease trypsin triggers induction of apoptosis in follicular papillae, which results in a delay in hair growth and pigmentation. *See Id.* at col. 2, last paragraph.

Although the high homology of PVP with serine proteases and the knowledge of serine proteases' role in keratinization are enough to reasonably correlate PVP's role with keratinization, Applicants provide even further support by showing that gene expression of PVP is increased when hair growth is perturbed in *whn*(-/-) mice, as opposed to two keratin genes, Ha3 and Ck15. This experimental evidence demonstrating a causal relationship in the regulation of PVP and hair keratinization only strengthens Applicant's assertion of PVP's role in hair regulation. See Specification, pg. 2, lines 20-22. The experimental evidence, combined with the homology relationships and the known role of proteases in keratinization provides sufficient support for a specific and substantial utility of the present application.

Based on the remarks above, Applicants respectfully request withdrawal of this rejection.

III. Claim Rejection Under 35 U.S.C. 112, First Paragraph:

The Examiner rejected claims 8, 9, 16-18 and 21 under 35 U.S.C. 112, first paragraph, as allegedly not providing guidance to one skilled in the art to make and use the claimed invention, based on the Examiner's contention that the claimed invention is not supported by either a credible asserted utility or a well-established utility. Applicants respectfully traverse this rejection.

The Examiner contends that any nucleotide sequence which hybridizes to SEQ ID NO:1 at 20 °C below the DNA melting point requires undue experimentation. See Office Action, pg. 4. Applicants have amended claim 8 to remove the limitation of hybridization to a complement of SEQ ID NO:1 at 20 °C below the DNA melting point. Applicants respectfully request that the rejection be withdrawn.

The Examiner further contends that the specification, based on the lack of utility, lack evidence of a causal relationship between the protease-related protein and regulation of the keratinization of hair. The Examiner also contends that "if the specification disclosed *in vivo* working examples to show this, then this may overcome the enablement rejection. However, since the specification does not show any *in vivo* working examples, it is not clear that the claimed method is enabled." See Office Action, pg. 4. For the reasons above regarding the assertion of utility in the instant application, Applicants respectfully disagree with the Examiner that the instant application fails to establish a causal relationship between the protease-related protein and regulation of the keratinization of hair based on an alleged lack of utility. In addition, for the reasons outlined below, Applicants respectfully disagree with the Examiner that working examples are required in order to enable the claimed invention.

Applicants wish to point out that the existence of working examples is only one of a lengthy list of factors that the Federal Circuit has suggested in determining whether the scope of claims in a patent application or patent are enabled by the disclosure. The list of the factors to be considered are:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Furthermore, the court in Wands states:

> It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. *In re Wands*, 858 F.2d 731 at 737,740 (Fed. Cir. 1988).

In regards to the absence of working examples, Applicants submit that they have provided sufficient guidance in the specification to one of ordinary skill in the art to make and use the claimed invention. The level of predictability for one of ordinary skill in the art is minimized due to the teachings of the nucleic acid and amino acid sequences necessary to perform the invention. The endpoints of the claimed invention are not highly unpredictable as the Examiner contends. One of ordinary skill in the art, without extensive assays or devices, can perform routine experimentation on a therapeutically effective level of the nucleic acid and amino acid sequence without undue experimentation, looking only for the growth of hair or lack thereof. In addition, Applicants respectfully point out that the test for undue experimentation itself "is not merely quantitative, since a considerable amount of experimentation is permissible if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention." *In re Wands*, 858 F.2d at 736-740. Applicants submit that the specification provides sufficient guidance to enable the amended claims in the instant application.

Claims 16, 17, and 18 have been revised for purposes of clarity.

Based on the amendment to the claims and the remarks above, Applicants respectfully request withdrawal of this rejection.

CONCLUSION

In light of the remarks and amendments set forth above, Applicant believes that the claims are in condition for allowance. Applicant respectfully solicits the Examiner to expedite the prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Date: May 16, 2005

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Office Action Response
U.S. Ser. No. 09/486,247

EXHIBIT A:

1. Kallikrein 6 – [Rattus norvegicus]

```
>gi|9506997|ref|NP_062048.1| G kallikrein 6 [Rattus norvegicus]
 gi|2853366|gb|AAC02300.1| G myelencephalon specific protease [Rattus
norvegicus]
          Length = 251

 Score =  492 bits (1266), Expect = e-138
 Identities = 223/251 (88%), Positives = 241/251 (96%)

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            MP KMLT+K LALCL+LAKSAWSE+Q+KVVHGGPCLK+SHPFQAALYTSGHLLCGGVL+
Sbjct: 1    MPTKMLTVKTLALCLILAKSAWSEDQDKVVHGGPCLKNSHPFQAALYTSGHLLCGGVLVG 60

Query: 61   PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
            PQWVLTAAHCKKPNL+V LGKHNLRQTETFQRQISVDRTIVHPRYNP+THDNDIMMVHLK
Sbjct: 61   PQWVLTAAHCKKPNLEVYLGKHNLRQTETFQRQISVDRTIVHPRYNPQTHDNDIMMVHLK 120

Query: 121  NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYP 180
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Sbjct: 121  RPVKFSQRIQPLPLKKDCSEKNPDCQILGWGKMENGEFPDTIQCADVQLVSREECERAYP 180

Query: 181  GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
            GKIT+SMVCAGD +EGNDSCQGDSGGPLVCGG LRG+VSWGDMPCGSKEKPGVYTDVCTH
Sbjct: 181  GKITRSMVCAGDKREGNDSCQGDSGGPLVCGGHLRGIVSWGDMPCGSKEKPGVYTDVCTH 240

Query: 241  IRWIQNILRNK 251
            IRWIQNI+RNK
Sbjct: 241  IRWIQNIIRNK 251
```

☐1: NP_062048. Reports kallikrein 6 [Rat...[gi:9506997] BLink, Domains, Links

```
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DEFINITION  kallikrein 6 [Rattus norvegicus].
ACCESSION   NP_062048
VERSION     NP_062048.1  GI:9506997
DBSOURCE    REFSEQ: accession NM_019175.1
KEYWORDS    .
SOURCE      Rattus norvegicus (Norway rat)
  ORGANISM  Rattus norvegicus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muridae; Murinae; Rattus.
REFERENCE   1  (residues 1 to 251)
  AUTHORS   Scarisbrick,I.A., Towner,M.D. and Isackson,P.J.
  TITLE     Nervous system-specific expression of a novel serine protease:
            regulation in the adult rat spinal cord by excitotoxic injury
  JOURNAL   J. Neurosci. 17 (21), 8156-8168 (1997)
   PUBMED   9334391
COMMENT     PROVISIONAL REFSEQ: This record has not yet been subject to final
            NCBI review. The reference sequence was derived from AF016269.1.

            SUMMARY: a myelencephalon-specific protease which has trypsin-like
            substrate specificity; expressed in the nervous system [RGD].
FEATURES             Location/Qualifiers
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                     /chromosome="1"
                     /map="1q22"
     Protein         1..251
                     /product="kallikrein 6"
                     /note="kallikrein 6 (neurosin); kallikrein 6 (neurosin
                     zyme); protease serine 9; protease serine 9 (neurosin);
                     protease, serine, 9; kallikrein 6 (neurosin, zyme)"
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                     /coded_by="NM_019175.1:185..940"
                     /note="go_function: tissue kallikrein activity [goid
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                     /db_xref="GeneID:29245"
                     /db_xref="RGD:3419"
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      241 irwiqniirn k
//
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1: AF016269. Reports Rattus norvegicus...[gi:2853365] Links

```
LOCUS       AF016269                1110 bp    mRNA    linear   ROD 11-FEB-1998
DEFINITION  Rattus norvegicus myelencephalon specific protease mRNA, complete
            cds.
ACCESSION   AF016269
VERSION     AF016269.1  GI:2853365
KEYWORDS    .
SOURCE      Rattus norvegicus (Norway rat)
  ORGANISM  Rattus norvegicus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muridae; Murinae; Rattus.
REFERENCE   1  (bases 1 to 1110)
  AUTHORS   Scarisbrick,I.A., Towner,M.D. and Isackson,P.J.
  TITLE     Nervous system-specific expression of a novel serine protease:
            regulation in the adult rat spinal cord by excitotoxic injury
  JOURNAL   J. Neurosci. 17 (21), 8156-8168 (1997)
   PUBMED   9334391
REFERENCE   2  (bases 1 to 1110)
  AUTHORS   Scarisbrick,I.A., Towner,M.D. and Isackson,P.J.
  TITLE     Direct Submission
  JOURNAL   Submitted (28-JUL-1997) Molecular Neuroscience, Mayo Foundation,
            200 First St., SW, Rochester, MN 55905, USA
FEATURES             Location/Qualifiers
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                     /mol_type="mRNA"
                     /strain="Sprague-Dawley"
                     /db_xref="taxon:10116"
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                     /product="myelencephalon specific protease"
                     /protein_id="AAC02300.1"
                     /db_xref="GI:2853366"
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                     SWGDMPCGSKEKPGVYTDVCTHIRWIQNIIRNK"
ORIGIN
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       61 tgtcagtctg ctctgcccct tctcttgtgg agcaccctgc cttgctgact ttctctgcct
      121 gtgataggtg gtgtcgtttc ccccccacct aagttctggc aggtacactg ctggccagca
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 181 gcagatgccc acgaagatgc tgacagtgaa gacgctggcc ctgtgcttga ttcttgctaa
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 301 tcaccctttc caagctgccc tctacacctc gggtcacttg ctgtgtggtg gggtcctcgt
 361 cggcccacag tgggtgctga cagctgccca ctgcaaaaaa ccgaatctgg aggtgtactt
 421 ggggaaacac aatctacggc aaactgagac tttccaaagg caaatctctg tggacaggac
 481 tattgtccat ccccgttaca atccccaaac ccatgacaat gatatcatga tggtgcatct
 541 gaaacgtcca gtcaaattct ctcaaaggat ccagcccctg cctttgaaga aagactgctc
 601 tgagaagaat cccgactgtc agatcctcgg ctggggcaag atggaaaacg gtgaattccc
 661 agataccatc cagtgtgctg atgtccagct ggtgtcccgg gaagagtgtg agcgcgccta
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 841 atggggtgac atgccctgtg gatcaaagga aaagccggga gtttacacag atgtctgcac
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1021 gccccactct cagagccttc agatgtccag ctctgccccc tcatgcttaa taaatgcagt
1081 gaaaaaaaaa aaaaaaaaaa aaaaaaaaaa
//
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U.S. Ser. No. 09/486,247
Exhibit A

2. Kallikrein 8, isoform 2 [Homo sapiens]

```
>gi|21464127|ref|NP_653088.1|  kallikrein 8 isoform 2 [Homo sapiens]
 gi|5672479|dbj|BAA82666.1|  neuropsin type2 [Homo sapiens]
          Length = 305

 Score =  238 bits (608), Expect = 8e-62
 Identities = 108/232 (46%), Positives = 158/232 (68%), Gaps = 6/232 (2%)

Query: 25  EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNL 84
            +++KV+ G  C   S P+QAAL+    LLCGGVL+    WVLTAAHCKKP   V LG H+L
Sbjct: 74  QEDKVLGGHECQPHSQPWQAALFQGQQLLCGGVLVGGNWVLTAAHCKKPKYTVRLGDHSL 133

Query: 85  RQTETFQRQISVDRTIVHPRYNP---ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEE 141
            +  +  +++I V ++I HP YN    E H++D+M++ L++      K++P+ L + C++
Sbjct: 134 QNKDGPEQEIPVVQSIPHPCYNSSDVEDHNHDLMLLQLRDQASLGSKVKPISLADHCTQP 193

Query: 142 NPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDS 199
               C + GWG + +   +FPDT+ CA+V + P+++CE AYPG+IT  MVCAG  K G D+
Sbjct: 194 GQKCTVSGWGTVTSPRENFPDTLNCAEVKIFPQKKCEDAYPGQITDGMVCAGSSK-GADT 252

Query: 200 CQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRNK 251
            CQGDSGGPLVC G L+G+ SWG  PCG  +KPGVYT++C ++ WI+ I+ +K
Sbjct: 253 CQGDSGGPLVCDGALQGITSWGSDPCGRSDKPGVYTNICRYLDWIKKIIGSK 304
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1: NP_653088. Reports kallikrein 8 isof...[gi:21464127] BLink, Domains, Links

```
LOCUS       NP_653088                305 aa            linear   PRI 26-JAN-2005
DEFINITION  kallikrein 8 isoform 2 [Homo sapiens].
ACCESSION   NP_653088
VERSION     NP_653088.1  GI:21464127
DBSOURCE    REFSEQ: accession NM_144505.1
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 305)
  AUTHORS   Li,Y., Qian,Y.P., Yu,X.J., Wang,Y.Q., Dong,D.G., Sun,W., Ma,R.M.
            and Su,B.
  TITLE     Recent origin of a hominoid-specific splice form of neuropsin, a
            gene involved in learning and memory
  JOURNAL   Mol. Biol. Evol. 21 (11), 2111-2115 (2004)
   PUBMED   15282331
REFERENCE   2  (residues 1 to 305)
  AUTHORS   Shigemasa,K., Tian,X., Gu,L., Tanimoto,H., Underwood,L.J.,
            O'Brien,T.J. and Ohama,K.
  TITLE     Human kallikrein 8 (hK8/TADG-14) expression is associated with an
            early clinical stage and favorable prognosis in ovarian cancer
  JOURNAL   Oncol. Rep. 11 (6), 1153-1159 (2004)
   PUBMED   15138549
  REMARK    GeneRIF: Expression of hK8 is increased during the development of
            ovarian cancer and down-regulated during ovarian cancer
            progression.
REFERENCE   3  (residues 1 to 305)
  AUTHORS   Can, Bignotti,E., Bellone,S., Palmieri,M., De las Casas,L.,
            Roman,J.J., Pecorelli,S., Cannon,M.J., O'brien,T. and Santin,A.D.
  TITLE     The novel serine protease tumor-associated differentially expressed
            gene-14 (KLK8/Neuropsin/Ovasin) is highly overexpressed in cervical
            cancer
  JOURNAL   Am. J. Obstet. Gynecol. 190 (1), 60-66 (2004)
   PUBMED   14749636
  REMARK    GeneRIF: Cervical cancer expressed high level of TADG-14. May play
            important role in invasion and metastasis. Appears only in
            abundance in tumor tissue and contains secretion signal sequence.
            Possible diagnostic use or as therapeutic target.
REFERENCE   4  (residues 1 to 305)
  AUTHORS   Clark,H.F., Gurney,A.L., Abaya,E., Baker,K., Baldwin,D., Brush,J.,
            Chen,J., Chow,B., Chui,C., Crowley,C., Currell,B., Deuel,B.,
            Dowd,P., Eaton,D., Foster,J., Grimaldi,C., Gu,Q., Hass,P.E.,
            Heldens,S., Huang,A., Kim,H.S., Klimowski,L., Jin,Y., Johnson,S.,
            Lee,J., Lewis,L., Liao,D., Mark,M., Robbie,E., Sanchez,C.,
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            Schoenfeld,J., Seshagiri,S., Simmons,L., Singh,J., Smith,V.,
            Stinson,J., Vagts,A., Vandlen,R., Watanabe,C., Wieand,D., Woods,K.,
            Xie,M.H., Yansura,D., Yi,S., Yu,G., Yuan,J., Zhang,M., Zhang,Z.,
            Goddard,A., Wood,W.I., Godowski,P. and Gray,A.
  TITLE     The secreted protein discovery initiative (SPDI), a large-scale
            effort to identify novel human secreted and transmembrane proteins:
            a bioinformatics assessment
  JOURNAL   Genome Res. 13 (10), 2265-2270 (2003)
   PUBMED   12975309
REFERENCE   5  (residues 1 to 305)
  AUTHORS   Magklara,A., Scorilas,A., Katsaros,D., Massobrio,M., Yousef,G.M.,
            Fracchioli,S., Danese,S. and Diamandis,E.P.
  TITLE     The human KLK8 (neuropsin/ovasin) gene: identification of two novel
            splice variants and its prognostic value in ovarian cancer
  JOURNAL   Clin. Cancer Res. 7 (4), 806-811 (2001)
   PUBMED   11309326
REFERENCE   6  (residues 1 to 305)
  AUTHORS   Harvey,T.J., Hooper,J.D., Myers,S.A., Stephenson,S.A.,
            Ashworth,L.K. and Clements,J.A.
  TITLE     Tissue-specific expression patterns and fine mapping of the human
            kallikrein (KLK) locus on proximal 19q13.4
  JOURNAL   J. Biol. Chem. 275 (48), 37397-37406 (2000)
   PUBMED   10969073
REFERENCE   7  (residues 1 to 305)
  AUTHORS   Gan,L., Lee,I., Smith,R., Argonza-Barrett,R., Lei,H., McCuaig,J.,
            Moss,P., Paeper,B. and Wang,K.
  TITLE     Sequencing and expression analysis of the serine protease gene
            cluster located in chromosome 19q13 region
  JOURNAL   Gene 257 (1), 119-130 (2000)
   PUBMED   11054574
REFERENCE   8  (residues 1 to 305)
  AUTHORS   Underwood,L.J., Tanimoto,H., Wang,Y., Shigemasa,K., Parmley,T.H.
            and O'Brien,T.J.
  TITLE     Cloning of tumor-associated differentially expressed gene-14, a
            novel serine protease overexpressed by ovarian carcinoma
  JOURNAL   Cancer Res. 59 (17), 4435-4439 (1999)
   PUBMED   10485494
REFERENCE   9  (residues 1 to 305)
  AUTHORS   Mitsui,S., Tsuruoka,N., Yamashiro,K., Nakazato,H. and Yamaguchi,N.
  TITLE     A novel form of human neuropsin, a brain-related serine protease,
            is generated by alternative splicing and is expressed
            preferentially in human adult brain
  JOURNAL   Eur. J. Biochem. 260 (3), 627-634 (1999)
   PUBMED   10102990
REFERENCE   10 (residues 1 to 305)
  AUTHORS   Yoshida,S., Taniguchi,M., Hirata,A. and Shiosaka,S.
  TITLE     Sequence analysis and expression of human neuropsin cDNA and gene
  JOURNAL   Gene 213 (1-2), 9-16 (1998)
   PUBMED   9714609
COMMENT     REVIEWED REFSEQ: This record has been curated by NCBI staff. The
            reference sequence was derived from AB008927.1, AB009849.1 and
            AF095742.1.

            Summary: Kallikreins are a subgroup of serine proteases having
            diverse physiological functions. Growing evidence suggests that
            many kallikreins are implicated in carcinogenesis and some have
            potential as novel cancer and other disease biomarkers. This gene
            is one of the fifteen kallikrein subfamily members located in a
            cluster on chromosome 19. Alternate splicing of this gene results
            in four transcript variants encoding four different isoforms. The
```

```
          isoforms exhibit distinct patterns of expression that suggest roles
          in brain plasticity and ovarian cancer.

          Transcript Variant: This variant (2) uses an alternate in-frame
          splice site in the 5' coding region, compared to variant 1,
          resulting in a longer protein compared to isoform 1.
FEATURES             Location/Qualifiers
     source          1..305
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /chromosome="19"
                     /map="19q13.3-q13.4"
     Protein         1..305
                     /product="kallikrein 8 isoform 2"
                     /note="protease, serine, 19; neuropsin; ovasin;
                     tumor-associated differentially expressed gene 14;
                     neuropsin type 1; neuropsin type 2"
     CDS             1..305
                     /gene="KLK8"
                     /coded_by="NM_144505.1:180..1097"
                     /note="isoform 2 is encoded by transcript variant 2;
                     go_function: trypsin activity [goid 0004295] [evidence
                     IEA];
                     go_function: hydrolase activity [goid 0016787] [evidence
                     IEA];
                     go_function: peptidase activity [goid 0008233] [evidence
                     IEA];
                     go_function: chymotrypsin activity [goid 0004263]
                     [evidence IEA];
                     go_process: neurogenesis [goid 0007399] [evidence TAS]
                     [pmid 10102990];
                     go_process: proteolysis and peptidolysis [goid 0006508]
                     [evidence IEA]"
                     /db_xref="GeneID:11202"
                     /db_xref="MIM:605644"
ORIGIN
        1 mgrprpraak twmfllllgg awaacgsldl ltklyaenlp cvhlnpqwps qpshcprgwr
       61 snplppaagh sraqedkvlg ghecqphsqp wqaalfqgqq llcggvlvgg nwvltaahck
      121 kpkytvrlgd hslqnkdgpe qeipvvqsip hpcynssdve dhnhdlmllq lrdqaslgsk
      181 vkpisladhc tqpgqkctvs gwgtvtspre nfpdtlncae vkifpqkkce daypgqitdg
      241 mvcagsskga dtcqgdsggp lvcdgalqgi tswgsdpcgr sdkpgvytni cryldwikki
      301 igskg
//
```

U.S. Ser. No. 09/486,247
Exhibit A

3. Kallikrein 14 preproprotein [Homo sapiens]

```
>gi|11545747|ref|NP_071329.1|  kallikrein 14 preproprotein [Homo sapiens]
 gi|6715552|gb|AAD50773.2|  kallikrein-like protein 6 [Homo sapiens]
 gi|13897995|gb|AAK48524.1|  kallikrein 14 [Homo sapiens]
 gi|13897993|gb|AAK48523.1|  kallikrein 14 [Homo sapiens]
 gi|10799399|gb|AAG23260.1|  Homo sapiens kallikrein-like protein 6
 gi|12230294|sp|Q9P0G3|KLK14_HUMAN  Kallikrein 14 precursor (Kallikrein-like
protein 6) (KLK-L6)
          Length = 251

 Score =  238 bits (606), Expect = 1e-61
 Identities = 107/241 (44%), Positives = 156/241 (64%), Gaps = 4/241 (1%)

Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGH--LLCGGVLIDPQWVLTAAHCKK 72
            L +A +   E++ K++ G  C + S P+QAAL        LCGG L+  QWV+TAAHC +
Sbjct: 11  LAIAMTQSQEDENKIIGGHTCTRSSQPWQAALLAGPRRRFLCGGALLSGQWVITAAHCGR 70

Query: 73  PNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPL 132
            P LQV LGKHNLR+ E  Q+ + V R + HP YN  THDND+M++ L+ P +  + ++P+
Sbjct: 71  PILQVALGKHNLRRWEATQQVLRVVRQVTHPNYNSRTHDNDLMLLQLQQPARIGRAVRPI 130

Query: 133 PLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCA 190
             +    C+    +C++ GWG + +    +P ++QC ++++ P E C++AYP  IT  MVCA
Sbjct: 131 EVTQACASPGTSCRVSGWGTISSPIARYPASLQCVNINISPDEVCQKAYPRTITPGMVCA 190

Query: 191 GDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            G  + G DSCQGDSGGPLVC G+L+GLVSWG  C      PGVYT++C +  WI+  +R+
Sbjct: 191 GVPQGGKDSCQGDSGGPLVCRGQLQGLVSWGMERCALPGYPGVYTNLCKYRSWIEETMRD 250

Query: 251 K 251
            K
Sbjct: 251 K 251
```

1: NP_071329. Reports kallikrein 14 pre...[gi:11545747] BLink, Domains, Links

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LOCUS       NP_071329                251 aa            linear   PRI 02-MAR-2005
DEFINITION  kallikrein 14 preproprotein [Homo sapiens].
ACCESSION   NP_071329
VERSION     NP_071329.1  GI:11545747
DBSOURCE    REFSEQ: accession NM_022046.3
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (residues 1 to 251)
  AUTHORS   Yousef,G.M., Stephan,C., Scorilas,A., Ellatif,M.A., Jung,K.,
            Kristiansen,G., Jung,M., Polymeris,M.E. and Diamandis,E.P.
  TITLE     Differential expression of the human kallikrein gene 14 (KLK14) in
            normal and cancerous prostatic tissues
  JOURNAL   Prostate 56 (4), 287-292 (2003)
   PUBMED   12858357
  REMARK    GeneRIF: KLK14 expression upregulated in advanced and more
            aggressive prostate tumors; may play role in tumor spread and may
            be new marker for prostate cancer diagnosis and prognosis
REFERENCE   2  (residues 1 to 251)
  AUTHORS   Yousef,G.M., Borgono,C.A., Scorilas,A., Ponzone,R., Biglia,N.,
            Iskander,L., Polymeris,M.E., Roagna,R., Sismondi,P. and
            Diamandis,E.P.
  TITLE     Quantitative analysis of human kallikrein gene 14 expression in
            breast tumours indicates association with poor prognosis
  JOURNAL   Br. J. Cancer 87 (11), 1287-1293 (2002)
   PUBMED   12439719
  REMARK    GeneRIF: KLK14 overexpression was found to be a significant
            predictor of decreased disease-free survival and overall survival
            in breast cancer patients
REFERENCE   3  (residues 1 to 251)
  AUTHORS   Yousef,G.M., Magklara,A., Chang,A., Jung,K., Katsaros,D. and
            Diamandis,E.P.
  TITLE     Cloning of a new member of the human kallikrein gene family, KLK14,
            which is down-regulated in different malignancies
  JOURNAL   Cancer Res. 61 (8), 3425-3431 (2001)
   PUBMED   11309303
REFERENCE   4  (residues 1 to 251)
  AUTHORS   Hooper,J.D., Bui,L.T., Rae,F.K., Harvey,T.J., Myers,S.A.,
            Ashworth,L.K. and Clements,J.A.
  TITLE     Identification and characterization of KLK14, a novel kallikrein
            serine protease gene located on human chromosome 19q13.4 and
            expressed in prostate and skeletal muscle
```

```
  JOURNAL   Genomics 73 (1), 117-122 (2001)
   PUBMED   11352573
REFERENCE   5  (residues 1 to 251)
  AUTHORS   Harvey,T.J., Hooper,J.D., Myers,S.A., Stephenson,S.A.,
            Ashworth,L.K. and Clements,J.A.
  TITLE     Tissue-specific expression patterns and fine mapping of the human
            kallikrein (KLK) locus on proximal 19q13.4
  JOURNAL   J. Biol. Chem. 275 (48), 37397-37406 (2000)
   PUBMED   10969073
COMMENT     REVIEWED REFSEQ: This record has been curated by NCBI staff. The
            reference sequence was derived from AF283670.1 and AF161221.1.

            Summary: Kallikreins are a subgroup of serine proteases having
            diverse physiological functions. Growing evidence suggests that
            many kallikreins are implicated in carcinogenesis and some have
            potential as novel cancer and other disease biomarkers. This gene
            is one of the fifteen kallikrein subfamily members located in a
            cluster on chromosome 19. An additional transcript variant has been
            described but its full length nature has not been determined.
FEATURES             Location/Qualifiers
     source          1..251
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /chromosome="19"
                     /map="19q13.3-q13.4"
     Protein         1..251
                     /product="kallikrein 14 preproprotein"
                     /note="kallikrein-like protein 6"
     CDS             1..251
                     /gene="KLK14"
                     /coded_by="NM_022046.3:268..1023"
                     /db_xref="CCDS:CCDS12823.1"
                     /db_xref="GeneID:43847"
                     /db_xref="MIM:606135"
ORIGIN
        1 mflllltalqv laiamtqsqe denkiigght ctrssqpwqa allagprrrf lcggallsgq
       61 wvitaahcgr pilqvalgkh nlrrweatqq vlrvvrqvth pnynsrthdn dlmllqlqqp
      121 arigravrpi evtqacaspg tscrvsgwgt isspiarypa slqcvninis pdevcqkayp
      181 rtitpgmvca gvpqggkdsc qgdsggplvc rgqlqglvsw gmercalpgy pgvytnlcky
      241 rswieetmrd k
//
```

Disclaimer | Write to the Help Desk
NCBI | NLM | NIH

Feb 9 2005 14:31:10

U.S. Ser. No. 09/486,247
Exhibit A

4. KLK (kallikrein) 15 [Saguinus oedipus]

```
>gi|42759849|gb|AAS45302.1|   KLK15 [Saguinus oedipus]
        Length = 255

 Score =  221 bits (564), Expect = 1e-56
 Identities = 100/252 (39%), Positives = 154/252 (61%), Gaps = 14/252 (5%)

Query: 10  MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            +L L  +L  +A  ++  K++ G  C   S P+Q ALY  G   CG  LI P WVL+AAH
Sbjct: 4   LLPLSFLLTSTA--QDGGKLLEGEECAPHSQPWQVALYERGRFNCGASLISPHWVLSAAH 61

Query: 70  CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C+   ++V LG+HNLR+ +   ++  +  R I HPRY   +H +DIM++ L  P + + ++
Sbjct: 62  CQSRFMRVRLGEHNLRKRDGPEQLRTASRVIPHPRYEARSHRHDIMLLRLVQPARLTPQV 121

Query: 130 QPLPLKNDCSEENPNCQILGWGKMENGD------------FPDTIQCADVHLVPREQCER 177
            +P+ L   C       C + GWG + + +             PDT+ CA++ ++    C++
Sbjct: 122 RPVVLPTRCPHPGEACVVSGWGLVSHNEPGTTGRPQSQVSLPDTLHCANISIISDASCDK 181

Query: 178 AYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDV 237
             YPG++T +MVCAG    G +SC+GDSGGPLVCGG L+G+VSWGD+PC +   KPGVYT V
Sbjct: 182 NYPGRLTNTMVCAGAEGRGAESCEGDSGGPLVCGGILQGIVSWGDVPCDNTTKPGVYTKV 241

Query: 238 CTHIRWIQNILR 249
            C +++WI+  ++
Sbjct: 242 CRYVKWIRETMK 253
```

1: AAS45302. Reports KLK15 [Saguinus o...[gi:42759849] BLink, Domains, Links

```
LOCUS       AAS45302                 255 aa            linear   PRI 23-FEB-2004
DEFINITION  KLK15 [Saguinus oedipus].
ACCESSION   AAS45302
VERSION     AAS45302.1  GI:42759849
DBSOURCE    accession AF173845.2
KEYWORDS    .
SOURCE      Saguinus oedipus (cotton-top tamarin)
  ORGANISM  Saguinus oedipus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Platyrrhini;
            Callitrichidae; Saguinus.
REFERENCE   1  (residues 1 to 255)
  AUTHORS   Olsson,A.Y., Persson,A.M., Valtonen-Andre,C. and Lundwall,A.
  TITLE     Glandular kallikreins of the cotton-top tamarin: molecular cloning
            of the gene encoding the tissue kallikrein
  JOURNAL   DNA Cell Biol. 19 (12), 721-727 (2000)
   PUBMED   11177570
REFERENCE   2  (residues 1 to 255)
  AUTHORS   Olsson,Y., Persson,M. and Lundwall,A.
  TITLE     Direct Submission
  JOURNAL   Submitted (29-JUL-1999) Clinical Chemistry, Lund University,
            University Hospital, Malmo S-205 02, Sweden
REFERENCE   3  (residues 1 to 255)
  AUTHORS   Olsson,Y., Persson,M. and Lundwall,A.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-FEB-2004) Clinical Chemistry, Lund University,
            University Hospital, Malmo S-205 02, Sweden
  REMARK    Sequence update by submitter
COMMENT     Method: conceptual translation.
FEATURES             Location/Qualifiers
     source          1..255
                     /organism="Saguinus oedipus"
                     /db_xref="taxon:9490"
     Protein         1..255
                     /product="KLK15"
                     /name="prostin"
     CDS             1..255
                     /coded_by="join(AF173845.2:752..794,AF173845.2:4071..4221,
                     AF173845.2:4716..4999,AF173845.2:5120..5256,
                     AF173845.2:5931..6083)"
ORIGIN
        1 mwlllplsfl ltstaqdggk llegeecaph sqpwqvalye rgrfncgasl isphwvlsaa
       61 hcqsrfmrvr lgehnlrkrd gpeqlrtasr viphpryear shrhdimllr lvqparltpq
      121 vrpvvlptrc phpgeacvvs gwglvshnep gttgrpqsqv slpdtlhcan isiisdascd
      181 knypgrltnt mvcagaegrg aescegdsgg plvcggilqg ivswgdvpcd nttkpgvytk
```

```
    241 vcryvkwire tmkrn
//
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Feb 9 2005 14:31:10

U.S. Ser. No. 09/486,247
Exhibit A

5. Kallikrein 11 isoform 2 precursor [Homo sapiens]

```
>gi|21618357|ref|NP_659196.1|  G kallikrein 11 isoform 2 precursor [Homo
sapiens]
 gi|3649791|dbj|BAA33404.1|  G serine protease (TLSP) [Homo sapiens]
 gi|8574439|dbj|BAA96797.1|  G prostate-type hippostasin [Homo sapiens]
          Length = 282

 Score =  221 bits (563), Expect = 1e-56
 Identities = 104/249 (41%), Positives = 151/249 (60%), Gaps = 6/249 (2%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
             M++L L L+    +       + +++ G   C    S P+QAAL+     LLCG   LI P+W+LTA
Sbjct: 33   MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTA 92

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----ETHDNDIMMVHLKNPV 123
             AHC KP    V LG+HNL++ E   ++   +    +   HP +N      + H NDIM+V + +PV
Sbjct: 93   AHCLKPRYIVHLGQHNLQKEEGCEQTRTATESFPHPGFNNSLPNKDHRNDIMLVKMASPV 152

Query: 124  KFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPG 181
               +  ++PL L + C       +C I GWG    +      P T++CA++ ++   ++CE AYPG
Sbjct: 153  SITWAVRPLTLSSRCVTAGTSCLISGWGSTSSPQLRLPHTLRCANITIIEHQKCENAYPG 212

Query: 182  KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHI 241
              IT +MVCA    + G DSCQGDSGGPLVC    L+G++SWG   PC     KPGVYT VC ++
Sbjct: 213  NITDTMVCASVQEGGKDSCQGDSGGPLVCNQSLQGIISWGQDPCAITRKPGVYTKVCKYV 272

Query: 242  RWIQNILRN 250
              WIQ  ++N
Sbjct: 273  DWIQETMKN 281
```

1: NP_659196. Reports kallikrein 11 iso...[gi:21618357]


```
LOCUS       NP_659196                282 aa            linear   PRI 02-MAR-2005
DEFINITION  kallikrein 11 isoform 2 precursor [Homo sapiens].
ACCESSION   NP_659196
VERSION     NP_659196.1  GI:21618357
DBSOURCE    REFSEQ: accession NM_144947.1
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (residues 1 to 282)
  AUTHORS   Shigemasa,K., Gu,L., Tanimoto,H., O'Brien,T.J. and Ohama,K.
  TITLE     Human kallikrein gene 11 (KLK11) mRNA overexpression is associated
            with poor prognosis in patients with epithelial ovarian cancer
  JOURNAL   Clin. Cancer Res. 10 (8), 2766-2770 (2004)
   PUBMED   15102682
  REMARK    GeneRIF: KLK11 expression may play an important role in ovarian
            cancer development
REFERENCE   2  (residues 1 to 282)
  AUTHORS   Clark,H.F., Gurney,A.L., Abaya,E., Baker,K., Baldwin,D., Brush,J.,
            Chen,J., Chow,B., Chui,C., Crowley,C., Currell,B., Deuel,B.,
            Dowd,P., Eaton,D., Foster,J., Grimaldi,C., Gu,Q., Hass,P.E.,
            Heldens,S., Huang,A., Kim,H.S., Klimowski,L., Jin,Y., Johnson,S.,
            Lee,J., Lewis,L., Liao,D., Mark,M., Robbie,E., Sanchez,C.,
            Schoenfeld,J., Seshagiri,S., Simmons,L., Singh,J., Smith,V.,
            Stinson,J., Vagts,A., Vandlen,R., Watanabe,C., Wieand,D., Woods,K.,
            Xie,M.H., Yansura,D., Yi,S., Yu,G., Yuan,J., Zhang,M., Zhang,Z.,
            Goddard,A., Wood,W.I., Godowski,P. and Gray,A.
  TITLE     The secreted protein discovery initiative (SPDI), a large-scale
            effort to identify novel human secreted and transmembrane proteins:
            a bioinformatics assessment
  JOURNAL   Genome Res. 13 (10), 2265-2270 (2003)
   PUBMED   12975309
REFERENCE   3  (residues 1 to 282)
  AUTHORS   Borgono,C.A., Fracchioli,S., Yousef,G.M., Rigault de la
            Longrais,I.A., Luo,L.Y., Soosaipillai,A., Puopolo,M., Grass,L.,
            Scorilas,A., Diamandis,E.P. and Katsaros,D.
  TITLE     Favorable prognostic value of tissue human kallikrein 11 (hK11) in
            patients with ovarian carcinoma
  JOURNAL   Int. J. Cancer 106 (4), 605-610 (2003)
   PUBMED   12845660
  REMARK    GeneRIF: hK11 is a novel, independent marker of favorable prognosis
            in patients with ovarian cancer
REFERENCE   4  (residues 1 to 282)
```

```
  AUTHORS   Nakamura,T., Stephan,C., Scorilas,A., Yousef,G.M., Jung,K. and
            Diamandis,E.P.
  TITLE     Quantitative analysis of hippostasin/KLK11 gene expression in
            cancerous and noncancerous prostatic tissues
  JOURNAL   Urology 61 (5), 1042-1046 (2003)
   PUBMED   12736044
  REMARK    GeneRIF: There is a significant association between lower
            expression of prostate-type KLK11 and higher tumor stage, Gleason
            score, and tumor grade.
REFERENCE   5  (residues 1 to 282)
  AUTHORS   Nakamura,T., Mitsui,S., Okui,A., Miki,T. and Yamaguchi,N.
  TITLE     Molecular cloning and expression of a variant form of
            hippostasin/KLK11 in prostate
  JOURNAL   Prostate 54 (4), 299-305 (2003)
   PUBMED   12539228
  REMARK    GeneRIF: Hippostasin isoform 3 may play a role in the prostate,
            including reproductive and/or tumorigenic functions.
REFERENCE   6  (residues 1 to 282)
  AUTHORS   Diamandis,E.P., Okui,A., Mitsui,S., Luo,L.Y., Soosaipillai,A.,
            Grass,L., Nakamura,T., Howarth,D.J. and Yamaguchi,N.
  TITLE     Human kallikrein 11: a new biomarker of prostate and ovarian
            carcinoma
  JOURNAL   Cancer Res. 62 (1), 295-300 (2002)
   PUBMED   11782391
  REMARK    GeneRIF: Human kallikrein 11: a new biomarker of prostate and
            ovarian carcinoma.
REFERENCE   7  (residues 1 to 282)
  AUTHORS   Nakamura,T., Mitsui,S., Okui,A., Kominami,K., Nomoto,T.,
            Ukimura,O., Kawauchi,A., Miki,T. and Yamaguchi,N.
  TITLE     Alternative splicing isoforms of hippostasin (PRSS20/KLK11) in
            prostate cancer cell lines
  JOURNAL   Prostate 49 (1), 72-78 (2001)
   PUBMED   11550212
  REMARK    GeneRIF: may be useful marker for distinguishing prostate cancer
            and benign prostatic hypertrophy
REFERENCE   8  (residues 1 to 282)
  AUTHORS   Gan,L., Lee,I., Smith,R., Argonza-Barrett,R., Lei,H., McCuaig,J.,
            Moss,P., Paeper,B. and Wang,K.
  TITLE     Sequencing and expression analysis of the serine protease gene
            cluster located in chromosome 19q13 region
  JOURNAL   Gene 257 (1), 119-130 (2000)
   PUBMED   11054574
REFERENCE   9  (residues 1 to 282)
  AUTHORS   Mitsui,S., Yamada,T., Okui,A., Kominami,K., Uemura,H. and
            Yamaguchi,N.
  TITLE     A novel isoform of a kallikrein-like protease, TLSP/hippostasin,
            (PRSS20), is expressed in the human brain and prostate
  JOURNAL   Biochem. Biophys. Res. Commun. 272 (1), 205-211 (2000)
   PUBMED   10872828
REFERENCE   10 (residues 1 to 282)
  AUTHORS   Yousef,G.M., Scorilas,A. and Diamandis,E.P.
  TITLE     Genomic organization, mapping, tissue expression, and hormonal
            regulation of trypsin-like serine protease (TLSP PRSS20), a new
            member of the human kallikrein gene family
  JOURNAL   Genomics 63 (1), 88-96 (2000)
   PUBMED   10662548
REFERENCE   11 (residues 1 to 282)
  AUTHORS   Yoshida,S., Taniguchi,M., Suemoto,T., Oka,T., He,X. and Shiosaka,S.
  TITLE     cDNA cloning and expression of a novel serine protease, TLSP
  JOURNAL   Biochim. Biophys. Acta 1399 (2-3), 225-228 (1998)
```

```
   PUBMED   9765601
COMMENT     REVIEWED REFSEQ: This record has been curated by NCBI staff. The
            reference sequence was derived from AB041036.1 and BC022068.1.

            Summary: Kallikreins are a subgroup of serine proteases having
            diverse physiological functions. Growing evidence suggests that
            many kallikreins are implicated in carcinogenesis and some have
            potential as novel cancer and other disease biomarkers. This gene
            is one of the fifteen kallikrein subfamily members located in a
            cluster on chromosome 19. Alternate splicing of this gene results
            in two transcript variants encoding two different isoforms which
            are differentially expressed.

            Transcript Variant: This variant (2) encodes the longer isoform (2)
            which is preferentially expressed in prostate.
FEATURES             Location/Qualifiers
     source          1..282
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /chromosome="19"
                     /map="19q13.3-q13.4"
     Protein         1..282
                     /product="kallikrein 11 isoform 2 precursor"
                     /note="protease, serine, trypsin-like; protease, serine,
                     20 trypsin-like; hippostasin"
     mat_peptide     54..282
                     /product="kallikrein 11, isoform 2"
     CDS             1..282
                     /gene="KLK11"
                     /coded_by="NM_144947.1:113..961"
                     /note="isoform 2 precursor is encoded by transcript
                     variant 2"
                     /db_xref="CCDS:CCDS12818.1"
                     /db_xref="GeneID:11012"
                     /db_xref="MIM:604434"
ORIGIN
        1 mqrlrwlrdw kssgrgltaa kepgarsspl qamrilqlil lalatglvgg etriikgfec
       61 kphsqpwqaa lfektrllcg atliaprwll taahclkpry ivhlgqhnlq keegceqtrt
      121 atesfphpgf nnslpnkdhr ndimlvkmas pvsitwavrp ltlssrcvta gtsclisgwg
      181 stsspqlrlp htlrcaniti iehqkcenay pgnitdtmvc asvqeggkds cqgdsggplv
      241 cnqslqgiis wgqdpcaitr kpgvytkvck yvdwiqetmk nn
//
```


Feb 9 2005 14:31:10

U.S. Ser. No. 09/486,247
Exhibit A

6. Serine protease [Rattus rattus]

```
>gi|3559978|emb|CAA06643.1|   serine protease [Rattus rattus]
 gi|6093538|sp|O88780|NRPN_RAT   Neuropsin precursor (NP) (Kallikrein 8) (Brain
serine protease 1)
          Length = 260

 Score =  233 bits (594), Expect = 4e-60
 Identities = 110/245 (44%), Positives = 155/245 (63%), Gaps = 10/245 (4%)

Query: 13   LCLVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            + L L   AW+     +  K++ G  C   S P+Q AL+    L+CGGVL+  +WVLTAA
Sbjct: 13   ILLFLLMGAWAGLTRAQGSKILEGQECKPHSQPWQTALFQGERLVCGGVLVGDRWVLTAA 72

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRY---NPETHDNDIMMVHLKNPVKF 125
            HCKK    V LG H+L++ +  +++I V R+I HP +   NPE H +DIM++ L+N
Sbjct: 73   HCKKDKYSVRLGDHSLQKRDEPEQEIQVARSIQHPCFNSSNPEDHSHDIMLIRLQNSANL 132

Query: 126  SKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKI 183
              K++P+ L N C +    C I GWG + +   +FP+T+ CA+V +  + +CERAYPGKI
Sbjct: 133  GDKVKPIELANLCPKVGQKCIISGWGTVTSPQENFPNTLNCAEVKIYSQNKCERAYPGKI 192

Query: 184  TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
            T+ MVCAG    G D+CQGDSGGPLVC G L+G+ +WG  PCG  EKPGVYT +C +  W
Sbjct: 193  TEGMVCAGS-SNGADTCQGDSGGPLVCNGVLQGITTWGSDPCGKPEKPGVYTKICRYTNW 251

Query: 244  IQNIL 248
            I+  +
Sbjct: 252  IKKTM 256
```

NCBI Entrez Protein

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

Search Protein for Go Clear

Limits Preview/Index History Clipboard Details

Display GenPept Send all to file

Range: from begin to end Features: ☐ SNP ☐ CDD ☑ MGC ☐ HPRD

☐ 1: CAA06643. Reports serine protease [...[gi:3559978] BLink, Domains, Links

```
LOCUS       CAA06643                 260 aa            linear   ROD 07-SEP-1998
DEFINITION  serine protease [Rattus rattus].
ACCESSION   CAA06643
VERSION     CAA06643.1  GI:3559978
DBSOURCE    embl locus RRA5641, accession AJ005641.1
KEYWORDS    .
SOURCE      Rattus rattus (black rat)
  ORGANISM  Rattus rattus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muridae; Murinae; Rattus.
REFERENCE   1
  AUTHORS   Davies,B.J., Pickard,B.S., Steel,M., Morris,R.G. and Lathe,R.
  TITLE     Serine proteases in rodent hippocampus
  JOURNAL   J. Biol. Chem. 273 (36), 23004-23011 (1998)
   PUBMED   9722524
REFERENCE   2  (residues 1 to 260)
  AUTHORS   Lathe,R.
  TITLE     Direct Submission
  JOURNAL   Submitted (17-APR-1998) Lathe R., Ctr. for Genome Research and Ctr.
            for Neuroscience, University of Edinburgh, West Mains Road,
            Edinburgh, EH9 3JQ, UNITED KINGDOM
FEATURES             Location/Qualifiers
     source          1..260
                     /organism="Rattus rattus"
                     /strain="Fisher"
                     /db_xref="taxon:10117"
                     /clone="BSP1"
                     /tissue_type="brain"
                     /dev_stage="adult"
     Protein         1..260
                     /product="serine protease"
     sig_peptide     1..26
     mat_peptide     27..260
                     /product="serine protease"
     CDS             1..260
                     /gene="bsp1"
                     /coded_by="AJ005641.1:146..928"
                     /db_xref="GOA:O88780"
                     /db_xref="UniProt/Swiss-Prot:O88780"
ORIGIN
        1 mgrpppcaiq twillfllmg awagltraqg skilegqeck phsqpwqtal fqgerlvcgg
       61 vlvgdrwvlt aahckkdkys vrlgdhslqk rdepeqeiqv arsiqhpcfn ssnpedhshd
      121 imlirlqnsa nlgdkvkpie lanlcpkvgq kciisgwgtv tspqenfpnt lncaevkiys
      181 qnkceraypg kitegmvcag ssngadtcqg dsggplvcng vlqgittwgs dpcgkpekpg
```

```
      241 vytkicrytn wikktmgkrd
//
```

EXHIBIT A:

7. Serine Protease 19 [Mus musculus]

```
>gi|6679487|ref|NP_032966.1|  G protease, serine, 19 [Mus musculus]
 gi|33585579|gb|AAH55895.1|  G Protease, serine, 19 [Mus musculus]
 gi|7229069|dbj|BAA92435.1|  G neuropsin [Mus musculus]
 gi|6093537|sp|Q61955|NRPN_MOUSE  G Neuropsin precursor (NP) (Kallikrein 8)
 gi|1020091|dbj|BAA06451.1|  G neuropsin [Mus musculus]
 gi|1582323|prf||2118319A   neuropsin
          Length = 260

 Score =  239 bits (611), Expect = 4e-62
 Identities = 113/248 (45%), Positives = 159/248 (64%), Gaps = 10/248 (4%)

Query: 13   LCLVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
           + L+L   AW+      +  K++ G   C+   S P+QAAL+    L+CGGVL+   +WVLTAA
Sbjct: 13   ILLLLFMGAWAGLTRAQGSKILEGRECIPHSQPWQAALFQGERLICGGVLVGDRWVLTAA 72

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN---PETHDNDIMMVHLKNPVKF 125
           HCKK     V LG H+L+   +  +++I V  ++I HP YN    PE H +DIM++ L+N
Sbjct: 73   HCKKQKYSVRLGDHSLQSRDQPEQEIQVAQSIQHPCYNNSNPEDHSHDIMLIRLQNSANL 132

Query: 126  SKKIQPLPLKNDCSEENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKI 183
            K++P+ L N C +      C I GWG + +    +FP+T+ CA+V +  + +CERAYPGKI
Sbjct: 133  GDKVKPVQLANLCPKVGQKCIISGWGTVTSPQENFPNTLNCAEVKIYSQNKCERAYPGKI 192

Query: 184  TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
           T+ MVCAG    G D+CQGDSGGPLVC G L+G+ SWG  PCG  EKPGVYT +C +   W
Sbjct: 193  TEGMVCAGS-SNGADTCQGDSGGPLVCDGMLQGITSWGSDPCGKPEKPGVYTKICRYTTW 251

Query: 244  IQNILRNK 251
           I+  + N+
Sbjct: 252  IKKTMDNR 259
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NCBI Entrez Protein

PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Books

Search Protein for Go Clear

Limits Preview/Index History Clipboard Details

Display GenPept Send all to file

Range: from begin to end Features: SNP CDD MGC HPRD STS

1: NP_032966. Reports protease, serine,...[gi:6679487] BLink, Domains, Links

```
LOCUS       NP_032966                260 aa            linear   ROD 15-APR-2005
DEFINITION  protease, serine, 19 [Mus musculus].
ACCESSION   NP_032966
VERSION     NP_032966.1  GI:6679487
DBSOURCE    REFSEQ: accession NM_008940.1
KEYWORDS    .
SOURCE      Mus musculus (house mouse)
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1  (residues 1 to 260)
  AUTHORS   Terayama,R., Bando,Y., Takahashi,T. and Yoshida,S.
  TITLE     Differential expression of neuropsin and protease M/neurosin in
            oligodendrocytes after injury to the spinal cord
  JOURNAL   Glia 48 (2), 91-101 (2004)
   PUBMED   15378660
  REMARK    GeneRIF: study demonstrates changes in the expression of neuropsin
            and protease M/neurosin in oligodendrocytes following hemisection
            of the spinal cord
REFERENCE   2  (residues 1 to 260)
  AUTHORS   Matsumoto-Miyai,K., Ninomiya,A., Yamasaki,H., Tamura,H.,
            Nakamura,Y. and Shiosaka,S.
  TITLE     NMDA-dependent proteolysis of presynaptic adhesion molecule L1 in
            the hippocampus by neuropsin
  JOURNAL   J. Neurosci. 23 (21), 7727-7736 (2003)
   PUBMED   12944500
  REMARK    GeneRIF: Presynaptic adhesion molecule L1 is a substrate for
            neuropsin in the hippocampus.
REFERENCE   3  (residues 1 to 260)
  AUTHORS   Wong,G.W., Yang,Y., Yasuda,S., Li,L. and Stevens,R.L.
  TITLE     Mouse mast cells express the tryptic protease neuropsin/Prss19
  JOURNAL   Biochem. Biophys. Res. Commun. 303 (1), 320-325 (2003)
   PUBMED   12646205
  REMARK    GeneRIF: mouse MCs store at least two distinct families of
            tryptic-like proteases in their secretory granules, including
            PRSS19
REFERENCE   4  (residues 1 to 260)
  AUTHORS   Matsumoto-Miyai,K., Kitagawa,R., Ninomiya,A., Momota,Y., Yoshida,S.
            and Shiosaka,S.
  TITLE     Decidualization induces the expression and activation of an
            extracellular protease neuropsin in mouse uterus
  JOURNAL   Biol. Reprod. 67 (5), 1414-1418 (2002)
   PUBMED   12390870
  REMARK    GeneRIF: Neuropsin is the first extracellular protease to show the
```

```
            evident induction of expression and activity by decidualization and
            might contribute to the remodeling of extracellular components
            after decidualization.
REFERENCE   5  (residues 1 to 260)
  AUTHORS   Katsu,Y., Takasu,E. and Iguchi,T.
  TITLE     Estrogen-independent expression of neuropsin, a serine protease in
            the vagina of mice exposed neonatally to diethylstilbestrol
  JOURNAL   Mol. Cell. Endocrinol. 195 (1-2), 99-107 (2002)
   PUBMED   12354676
  REMARK    GeneRIF: gene expression of a serine-protease neuropsin in the
            mouse vagina, and as a marker of the estrogen-independent
            persistent proliferation and cornification of the vaginal
            epithelium
REFERENCE   6  (residues 1 to 260)
  AUTHORS   Oka,T., Hakoshima,T., Itakura,M., Yamamori,S., Takahashi,M.,
            Hashimoto,Y., Shiosaka,S. and Kato,K.
  TITLE     Role of loop structures of neuropsin in the activity of serine
            protease and regulated secretion
  JOURNAL   J. Biol. Chem. 277 (17), 14724-14730 (2002)
   PUBMED   11854276
  REMARK    GeneRIF: role of loop structures in the activity of serine protease
            and regulated secretion
REFERENCE   7  (residues 1 to 260)
  AUTHORS   Oka,T., Akisada,M., Okabe,A., Sakurai,K., Shiosaka,S. and Kato,K.
  TITLE     Extracellular serine protease neuropsin (KLK8) modulates neurite
            outgrowth and fasciculation of mouse hippocampal neurons in culture
  JOURNAL   Neurosci. Lett. 321 (3), 141-144 (2002)
   PUBMED   11880192
  REMARK    GeneRIF: Neuropsin was localized extracellularly in neuronal cell
            bodies and their neurites in mouse hippocampus. Neuropsin may be
            involved in neurite outgrowth during the development of the nervous
            system.
REFERENCE   8  (residues 1 to 260)
  AUTHORS   Chen,Z.L., Yoshida,S., Kato,K., Momota,Y., Suzuki,J., Tanaka,T.,
            Ito,J., Nishino,H., Aimoto,S., Kiyama,H. et al.
  TITLE     Expression and activity-dependent changes of a novel limbic-serine
            protease gene in the hippocampus
  JOURNAL   J. Neurosci. 15 (7 PT 2), 5088-5097 (1995)
   PUBMED   7623137
COMMENT     PROVISIONAL REFSEQ: This record has not yet been subject to final
            NCBI review. The reference sequence was derived from D30785.1.
FEATURES             Location/Qualifiers
     source          1..260
                     /organism="Mus musculus"
                     /strain="BALB/c"
                     /db_xref="taxon:10090"
                     /chromosome="7"
     Protein         1..260
                     /product="protease, serine, 19"
                     /note="Brain Serine protease 1; neuropsin"
     CDS             1..260
                     /gene="Prss19"
                     /coded_by="NM_008940.1:487..1269"
                     /note="go_function: hydrolase activity [goid 0016787]
                     [evidence IEA];
                     go_function: peptidase activity [goid 0008233] [evidence
                     IEA];
                     go_function: serine-type endopeptidase activity [goid
                     0004252] [evidence IEA];
                     go_process: negative regulation of blood coagulation [goid
```

```
                    0030195] [evidence IEA]"
                    /db_xref="GeneID:259277"
                    /db_xref="MGI:1343327"
ORIGIN
        1 mgrpppcaiq pwillllfmg awagltraqg skilegreci phsqpwqaal fqgerlicgg
       61 vlvgdrwvlt aahckkqkys vrlgdhslqs rdqpeqeiqv aqsiqhpcyn nsnpedhshd
      121 imlirlqnsa nlgdkvkpvq lanlcpkvgq kciisgwgtv tspqenfpnt lncaevkiys
      181 qnkceraypg kitegmvcag ssngadtcqg dsggplvcdg mlqgitswgs dpcgkpekpg
      241 vytkicrytt wikktmdnrd
//
```


Feb 9 2005 14:31:10

Office Action Response

U.S. Ser. No. 09/486,247

EXHIBIT A:

8. Trypsin Precursor [Xenopus laevis]

```
>gi|2499865|sp|P70059|TRY2_XENLA   Trypsin precursor
 gi|1621633|gb|AAB17274.1|  G trypsinogen [Xenopus laevis]
          Length = 244

 Score =  223 bits (567), Expect = 5e-57
 Identities = 105/243 (43%), Positives = 154/243 (63%), Gaps = 4/243 (1%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK L + ++L  +   E+ +K+V G  C K++ P+Q +L  +G+  CGG LI+ QWV++A
Sbjct: 1    MKFLVILVLLGAAVAFEDDDKIVGGFTCAKNAVPYQVSL-NAGYHFCGGSLINSQWVVSA 59

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K  +QV LG+HN+    E  ++ I    + I HP YN    DNDIM++ L    + S
Sbjct: 60   AHCYKSRIQVRLGEHNIALNEGTEQFIDSQKVIKHPNYNSRNLDNDIMLIKLSTTARLSA 119

Query: 128  KIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQ 185
             IQ +PL + C+    NC I GWG  + +G ++PD +QC +   ++   QC  +YPG+IT+
Sbjct: 120  NIQSVPLPSACASAGTNCLISGWGNTLSSGTNYPDLLQCLNAPILTDSQCSNSYPGEITK 179

Query: 186  SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            +M CAG +   G DSCQGDSGGP+VC G+L+G+VSWG   C   +  PGVYT VC   + WIQ
Sbjct: 180  NMFCAGFLAGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRNYPGVYTKVCNFVTWIQ 238

Query: 246  NIL 248
            + +
Sbjct: 239  STI 241
```

1: P70059. Reports Trypsin precursor...[gi:2499865] BLink, Domains, Links

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LOCUS       P70059                   244 aa            linear   VRT 01-MAY-2005
DEFINITION  Trypsin precursor.
ACCESSION   P70059
VERSION     P70059  GI:2499865
DBSOURCE    swissprot: locus TRY2_XENLA, accession P70059;
            class: standard.
            created: Nov 1, 1997.
            sequence updated: Nov 1, 1997.
            annotation updated: May 1, 2005.
            xrefs: U72330.1, AAB17274.1
            xrefs (non-sequence databases): HSSPP00760, SMRP70059,
            MEROPSS01.126, InterProIPR009003, InterProIPR001254,
            InterProIPR001314, PfamPF00089, PRINTSPR00722, SMARTSM00020,
            PROSITEPS50240, PROSITEPS00134, PROSITEPS00135
KEYWORDS    Calcium; Calcium-binding; Digestion; Hydrolase; Multigene family;
            Protease; Serine protease; Signal; Zymogen.
SOURCE      Xenopus laevis (African clawed frog)
  ORGANISM  Xenopus laevis
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Amphibia; Batrachia; Anura; Mesobatrachia; Pipoidea; Pipidae;
            Xenopodinae; Xenopus; Xenopus.
REFERENCE   1  (residues 1 to 244)
  AUTHORS   Wang,K., Lytle,L., Gan,L. and Hood,L.E.
  TITLE     Direct Submission
  JOURNAL   Submitted (??-SEP-1996)
  REMARK    NUCLEOTIDE SEQUENCE.
COMMENT     [CATALYTIC ACTIVITY] Preferential cleavage: Arg-|-Xaa, Lys-|-Xaa.
            [COFACTOR] Binds 1 calcium ion per subunit (By similarity).
            [SUBCELLULAR LOCATION] Extracellular.
            [SIMILARITY] Belongs to the peptidase S1 family.
FEATURES             Location/Qualifiers
     source          1..244
                     /organism="Xenopus laevis"
                     /db_xref="taxon:8355"
     Protein         1..244
                     /product="Trypsin precursor"
                     /EC_number="3.4.21.4"
     Region          1..15
                     /region_name="Signal"
                     /note="By similarity."
                     /evidence=not_experimental
     Region          16..21
                     /region_name="Propeptide"
                     /note="Activation peptide (By similarity)."
                     /evidence=not_experimental
```

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     Region          22..244
                     /region_name="Mature chain"
                     /note="Trypsin."
                     /evidence=experimental
     Bond            bond(28,158)
                     /bond_type="disulfide"
                     /note="By similarity."
                     /evidence=not_experimental
     Bond            bond(46,62)
                     /bond_type="disulfide"
                     /note="By similarity."
                     /evidence=not_experimental
     Site            61
                     /site_type="active"
                     /note="Charge relay system (By similarity)."
                     /evidence=not_experimental
     Site            73
                     /site_type="metal-binding"
                     /note="Calcium (By similarity)."
                     /evidence=not_experimental
     Site            75
                     /site_type="metal-binding"
                     /note="Calcium (via carbonyl oxygen) (By similarity)."
                     /evidence=not_experimental
     Site            83
                     /site_type="metal-binding"
                     /note="Calcium (By similarity)."
                     /evidence=not_experimental
     Site            105
                     /site_type="active"
                     /note="Charge relay system (By similarity)."
                     /evidence=not_experimental
     Bond            bond(130,231)
                     /bond_type="disulfide"
                     /note="By similarity."
                     /evidence=not_experimental
     Bond            bond(137,204)
                     /bond_type="disulfide"
                     /note="By similarity."
                     /evidence=not_experimental
     Bond            bond(169,183)
                     /bond_type="disulfide"
                     /note="By similarity."
                     /evidence=not_experimental
     Site            192
                     /site_type="unclassified"
                     /note="Required for specificity (By similarity)."
                     /evidence=not_experimental
     Bond            bond(194,218)
                     /bond_type="disulfide"
                     /note="By similarity."
                     /evidence=not_experimental
     Site            198
                     /site_type="active"
                     /note="Charge relay system (By similarity)."
                     /evidence=not_experimental
ORIGIN
        1 mkflvilvll gaavafeddd kivggftcak navpyqvsln agyhfcggsl insqwvvsaa
       61 hcyksriqvr lgehnialne gteqfidsqk vikhpnynsr nldndimlik lsttarlsan
      121 iqsvplpsac asagtnclis gwgntlssgt nypdllqcln apiltdsqcs nsypgeitkn
```

```
      181 mfcagflagg kdscqgdsgg pvvcngqlqg vvswgygcaq rnypgvytkv cnfvtwiqst
      241 issn
//
```


Feb 9 2005 14:31:10

S NCBI results of BLAST

BLASTP 2.2.10 [Oct-19-2004]

Reference:
Altschul, Stephen F., Thomas L. Madden, Alejandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman (1997), "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Res. 25:3389-3402.

RID: 1110912140-32509-164324574163.BLASTQ4

Query=
(253 letters)

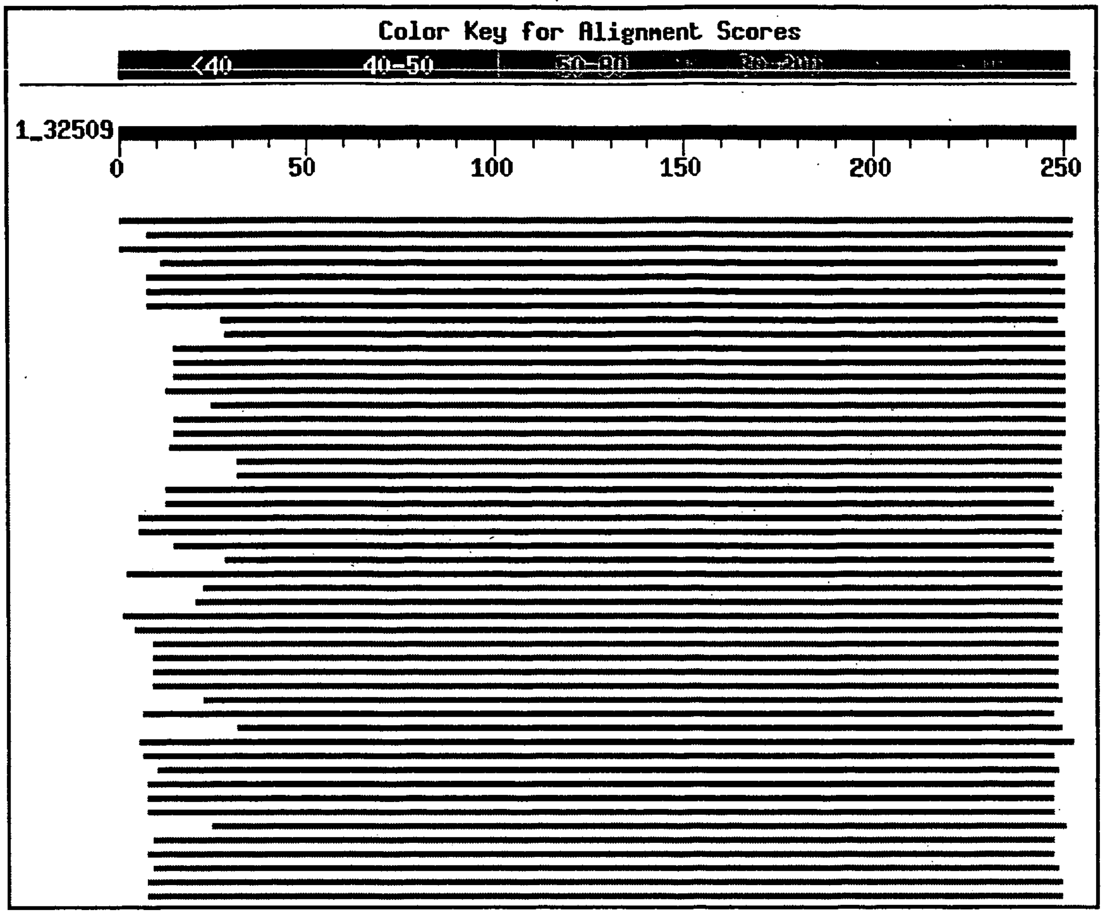
Database: All non-redundant GenBank CDS translations+PDB+SwissProt+PIR+PRF excluding environmental samples
2,366,628 sequences; 802,641,970 total letters

If you have any problems or questions with the results of this search please refer to the **BLAST FAQs**

Taxonomy reports

Distribution of 509 Blast Hits on the Query Sequence

Mouse-over to show defline and scores. Click to show alignments



Related Structures

Sequences producing significant alignments:		Score (bits)	E Value	
gi|21411424|gb|AAH31119.1|	Prss18 protein [Mus musculus] >g...	544	e-154	G
gi|6755180|ref|NP_035307.1|	protease, serine, 18 [Mus muscu...	530	e-149	G
gi|9506997|ref|NP_062048.1|	kallikrein 6 [Rattus norvegicus...	492	e-138	G
gi|57036286|ref|XP_533605.1|	PREDICTED: similar to Kallikre...	367	e-100	G
gi|15930186|gb|AAH15525.1|	KLK6 protein [Homo sapiens] >gi|...	366	e-100	G
gi|30585043|gb|AAP36794.1|	Homo sapiens kallikrein 6 (neuro...	366	e-100	
gi|55233182|gb|AAV48554.1|	kallikrein 6 preproprotein [synt...	366	e-100	
gi|21465525|pdb|1GVL|A	Chain A, Human Prokallikrein 6 (Hk6)...	347	1e-94	S
gi|21466131|pdb|1LO6|A	Chain A, Human Kallikrein 6 (Hk6) Ac...	346	4e-94	S
gi|37183190|gb|AAQ89395.1|	KLK8 [Homo sapiens] >gi|6005844|...	241	2e-62	G
gi|55649729|ref|XP_512847.1|	PREDICTED: similar to kallikre...	241	2e-62	G
gi|26454807|gb|AAH40887.1|	Kallikrein 8, isoform 1 prepropr...	240	3e-62	G
gi|6679487|ref|NP_032966.1|	protease, serine, 19 [Mus muscu...	239	4e-62	G
gi|21464127|ref|NP_653088.1|	kallikrein 8 isoform 2 [Homo s...	238	8e-62	G
gi|11545747|ref|NP_071329.1|	kallikrein 14 preproprotein [H...	238	1e-61	G
gi|50959826|gb|AAH74905.1|	Kallikrein 14, preproprotein [Ho...	237	2e-61	G
gi|34856166|ref|XP_218643.2|	similar to glandular kallikrei...	235	7e-61	G
gi|26891548|gb|AAN78420.1|	glandular kallikrein KLK13 [Mus ...	235	7e-61	G

gi|39645087|gb|AAH63763.1|	Unknown (protein for MGC:70078) ...	235	9e-61	
gi|27731521|ref|XP_218648.1|	similar to Neuropsin precursor...	234	2e-60	G
gi|3559978|emb|CAA06643.1|	serine protease [Rattus rattus] ...	233	4e-60	
gi|57037485|ref|XP_541468.1|	PREDICTED: similar to kallikre...	233	5e-60	G
gi|9910298|ref|NP_064358.1|	protease, serine, 20 [Mus muscu...	233	5e-60	G
gi|6681654|dbj|BAA36955.1|	hippostasin prostate type [Mus m...	233	5e-60	G
gi|4699765|pdb|1NPM|B	Chain B, Neuropsin, A Serine Protease...	233	5e-60	S
gi|33469049|ref|NP_777355.1|	kallikrein 14 [Mus musculus] >...	232	6e-60	G
gi|34856164|ref|XP_218641.2|	similar to glandular kallikrei...	231	1e-59	G
gi|28422450|gb|AAH44756.1|	Klk14 protein [Mus musculus]	230	2e-59	G
gi|34856172|ref|XP_218607.2|	similar to prostin [Rattus nor...	229	4e-59	G
gi|34856168|ref|XP_218645.2|	similar to hippostasin prostat...	228	9e-59	G
gi|11244759|gb|AAG33354.1|	ACO protease [Homo sapiens]	228	1e-58	G
gi|47480780|gb|AAH69507.1|	Kallikrein 15, isoform 4 preprop...	227	3e-58	G
gi|47480768|gb|AAH69480.1|	Kallikrein 15, isoform 4 preprop...	226	4e-58	G
gi|14484922|gb|AAK62813.1|	prostinogen [Homo sapiens]	226	6e-58	G
gi|12834991|dbj|BAB23113.1|	unnamed protein product [Mus mu...	225	1e-57	G
gi|57037473|ref|XP_541465.1|	PREDICTED: similar to glandula...	224	1e-57	G
gi|33585653|gb|AAH56068.1|	LOC397853 protein [Xenopus laevis]	224	1e-57	G
gi|33469045|ref|NP_777354.1|	kallikrein 15 [Mus musculus] >...	224	2e-57	G
gi|47481100|gb|AAH69334.1|	Kallikrein 13, precursor [Homo s...	224	2e-57	G
gi|49256006|gb|AAH73410.1|	LOC397853 protein [Xenopus laevis]	224	2e-57	G
gi|59808136|gb|AAH89741.1|	Unknown (protein for MGC:108396)...	224	2e-57	
gi|65163|emb|CAA37538.1|	unnamed protein product [Xenopus l...	223	3e-57	G
gi|32484229|gb|AAH54194.1|	MGC64344 protein [Xenopus laevis]	223	3e-57	G
gi|57037469|ref|XP_541464.1|	PREDICTED: similar to kallikre...	223	3e-57	G
gi|51714013|ref|XP_489832.1|	similar to trypsinogen 10 [Mus...	223	4e-57	G
gi|2499865|sp|P70059|TRY2_XENLA	Trypsin precursor >gi|16216...	223	5e-57	G
gi|42759849|gb|AAS45302.1|	KLK15 [Saguinus oedipus]	221	1e-56	
gi|37183146|gb|AAQ89373.1|	KLK11 [Homo sapiens] >gi|5803199...	221	1e-56	G
gi|21618357|ref|NP_659196.1|	kallikrein 11 isoform 2 precur...	221	1e-56	G
gi|51714016|ref|XP_489833.1|	similar to trypsinogen 12 [Mus...	221	2e-56	G
gi|6678439|ref|NP_033456.1|	protease, serine, 2 [Mus muscul...	220	3e-56	G
gi|57036282|ref|XP_533604.1|	PREDICTED: similar to kallikre...	220	3e-56	G
gi|58257843|gb|AAW69362.1|	try9 [Macaca mulatta]	219	4e-56	
gi|6981420|ref|NP_036767.1|	pancreatic trypsin 1 [Rattus no...	219	5e-56	G
gi|6755893|ref|NP_035776.1|	trypsin 4 [Mus musculus] >gi|23...	219	5e-56	G
gi|67548|pir||TRRT2	trypsin (EC 3.4.21.4) II precursor - rat	218	9e-56	
gi|6981422|ref|NP_036861.1|	protease, serine, 2 [Rattus nor...	218	1e-55	G
gi|47206216|emb|CAF90862.1|	unnamed protein product [Tetrao...	218	2e-55	
gi|51010909|ref|NP_001003405.1|	RIKEN cDNA 1810049H19 gene ...	217	2e-55	G
gi|16716569|ref|NP_444473.1|	trypsinogen 16 [Mus musculus] ...	217	3e-55	G
gi|28373261|pdb|1CO7|E	Chain E, R117h Mutant Rat Anionic Tr...	217	3e-55	S
gi|51871601|ref|NP_001004097.1|	trypsin 10 precursor [Rattu...	216	3e-55	G
gi|2358117|gb|AAB69087.1|	trypsinogen 15 [Mus musculus]	216	3e-55	
gi|758266|emb|CAA24581.1|	unnamed protein product [Rattus n...	216	5e-55	G
gi|34855584|ref|XP_342669.1|	similar to trypsinogen 9 [Ratt...	216	5e-55	G

gi|34855588|ref|XP_342672.1|	similar to trypsin (EC 3.4.21....	216	6e-55	G
gi|56541274|gb|AAH87610.1|	Hypothetical LOC496627 [Xenopus ...	216	6e-55	G
gi|51711962|ref|XP_487918.1|	PREDICTED: similar to trypsino...	215	8e-55	G
gi|27573668|pdb|1J14|A	Chain A, Benzamidine In Complex With...	215	8e-55	S
gi|4139560|pdb|3TGJ|E	Chain E, S195a Trypsinogen Complexed ...	215	1e-54	S
gi|14719441|pdb|1F7Z|A	Chain A, Rat Trypsinogen K15a Comple...	214	2e-54	S
gi|6755891|ref|NP_035775.1|	protease, serine, 3 [Mus muscul...	213	3e-54	G
gi|37182171|gb|AAQ88888.1|	KLK12 [Homo sapiens] >gi|2220898...	213	3e-54	G
gi|64388|emb|CAA49679.1|	trypsin III [Salmo salar] >gi|4225...	213	4e-54	
gi|27731519|ref|XP_218644.1|	similar to kallikrein 12 isofo...	213	4e-54	G
gi|27465583|ref|NP_775150.1|	cationic trypsinogen [Rattus n...	213	5e-54	G
gi|54035518|gb|AAH83528.1|	Zgc:92590 [Danio rerio] >gi|5574...	213	5e-54	G
gi|1633123|pdb|1SLW|B	Chain B, Rat Anionic N143h, E151h Try...	213	5e-54	S
gi|34855586|ref|XP_342670.1|	similar to trypsinogen 8 [Ratt...	212	7e-54	G
gi|1633121|pdb|1SLX|B	Chain B, Rat Anionic N143h, E151h Try...	212	7e-54	S
gi|57097397|ref|XP_532744.1|	PREDICTED: similar to trypsin ...	212	9e-54	G
gi|4139558|pdb|3TGI|E	Chain E, Wild-Type Rat Anionic Trypsi...	212	9e-54	S
gi|2098543|pdb|1AND|	Anionic Trypsin Mutant With Arg 96 Re...	212	9e-54	S
gi|559311|dbj|BAA07516.1|	pancreas cationic pretrypsinogen ...	211	1e-53	G S
gi|67549|pir||TRBOTR	trypsin (EC 3.4.21.4) precursor - bovi...	211	1e-53	S
gi|13096615|pdb|1G3E|A	Chain A, Bovine Beta-Trypsin Bound T...	211	1e-53	S
gi|5542503|pdb|1ZZZ|A	Chain A, Trypsin Inhibitors With Rigi...	211	1e-53	S
gi|1421532|pdb|1TGB|	Trypsinogen-Ca From Peg	211	1e-53	S
gi|17942679|pdb|1K9O|E	Chain E, Crystal Structure Of Michae...	211	2e-53	S
gi|2358083|gb|AAB69055.1|	trypsinogen 4 [Mus musculus] >gi|...	211	2e-53	G
gi|50054435|ref|NP_001001911.1|	kallikrein 1, renal/pancrea...	211	2e-53	G
gi|27819626|ref|NP_777115.1|	pancreatic anionic trypsinogen...	211	2e-53	G
gi|27545370|ref|NP_775423.1|	preprotrypsinogen IV [Rattus n...	210	2e-53	G
gi|67550|pir||TRPGTR	trypsin (EC 3.4.21.4) precursor - pig ...	210	2e-53	
gi|67552|pir||TRDG	trypsin (EC 3.4.21.4) precursor, anionic...	210	2e-53	
gi|51714019|ref|XP_489834.1|	similar to Try10-like trypsino...	210	2e-53	G
gi|6851258|gb|AAF29490.1|	tissue kallikrein [Saguinus oedipus]	210	2e-53	
gi|34810822|pdb|1OPH|B	Chain B, Non-Covalent Complex Betwee...	210	2e-53	S
gi|2098545|pdb|1ANC|	Anionic Trypsin Mutant With Ser 214 R...	210	2e-53	S
gi|2098541|pdb|1ANB|	Anionic Trypsin Mutant With Ser 214 R...	210	2e-53	S
gi|11513886|pdb|1FY8|E	Chain E, Crystal Structure Of The De...	210	3e-53	S
gi|9257000|pdb|1EZU|D	Chain D, Ecotin Y69f, D70p Bound To D...	210	3e-53	S
gi|2392288|pdb|1DPO|	Structure Of Rat Trypsin	210	3e-53	S
gi|230776|pdb|2TRM|	Asn102Trypsin (E.C.3.4.21.4) (Mutant W...	210	3e-53	S
gi|56541161|gb|AAH87563.1|	Unknown (protein for MGC:97681) ...	209	4e-53	G
gi|2781042|pdb|1AMH|B	Chain B, Uncomplexed Rat Trypsin Muta...	209	4e-53	S
gi|55649807|ref|XP_524358.1|	PREDICTED: similar to variant ...	209	6e-53	G
gi|58257847|gb|AAW69366.1|	try14 [Macaca mulatta]	209	6e-53	
gi|50979094|ref|NP_001003284.1|	kallikrein 2, prostatic [Ca...	209	7e-53	G
gi|45382397|ref|NP_990715.1|	trypsinogen [Gallus gallus] >g...	209	7e-53	G
gi|56971223|gb|AAH88079.1|	Hypothetical LOC496920 [Xenopus ...	209	7e-53	G

gi|25814806|gb|AAN75630.1| trypsinogen [Gallus gallus] 208 9e-53 G

gi|14719439|pdb|1F5R|A Chain A, Rat Trypsinogen Mutant Comp... 208 9e-53 S

gi|108957|pir||S13813 trypsin (EC 3.4.21.4) - bovine >gi|24... 208 1e-52

gi|108118|pir||A37938 tissue kallikrein (EC 3.4.21.35), pro... 208 1e-52 G

gi|2358072|gb|AAB69044.1| trypsinogen 7 [Mus musculus] >gi|... 208 1e-52 G

gi|56556311|gb|AAH87753.1| LOC496635 protein [Xenopus tropi... 208 1e-52 G

gi|14719487|pdb|3TGK|E Chain E, Trypsinogen Mutant D194n An... 208 1e-52 S

gi|57415|emb|CAA41752.1| trypsin V b-form [Rattus rattus] >... 207 2e-52

gi|27530958|dbj|BAC54105.1| variant form hippostasin/KLK11 ... 207 2e-52

gi|47220857|emb|CAG00064.1| unnamed protein product [Tetrao... 207 2e-52

gi|47220856|emb|CAG00063.1| unnamed protein product [Tetrao... 207 2e-52

gi|4389387|pdb|1A0J|D Chain D, Crystal Structure Of A Non-P... 207 2e-52 S

gi|2392548|pdb|1TAW|A Chain A, Bovine Trypsin Complexed To ... 207 2e-52 S

gi|60593451|pdb|1S0R|A Chain A, Bovine Pancreatic Trypsin I... 207 2e-52 S

gi|6981132|ref|NP_036725.1| kallikrein 7 [Rattus norvegicus... 207 2e-52 G

gi|2358071|gb|AAB69043.1| trypsinogen 5 [Mus musculus] 207 2e-52

gi|22652265|gb|AAN03662.1| kallikrein 7 long variant protei... 207 3e-52 G

gi|51094518|gb|EAL23773.1| protease, serine, 1 (trypsin 1) ... 207 3e-52 G

gi|230196|pdb|1NTP| Modified Beta Trypsin (Monoisopropylph... 207 3e-52 S

gi|27710074|ref|XP_231718.1| similar to Trypsin V-A precurs... 206 4e-52 G

gi|67551|pir||TRDGC trypsin (EC 3.4.21.4) precursor, cation... 206 4e-52

gi|10835849|pdb|1FNI|A Chain A, Crystal Structure Of Porcin... 206 4e-52 S

gi|576019|pdb|1BRC|E Chain E, Trypsin (E.C.3.4.21.4) Varian... 206 4e-52 S

gi|45382399|ref|NP_990716.1| trypsinogen [Gallus gallus] >g... 206 5e-52 G

gi|51746022|ref|XP_355892.2| RIKEN cDNA 2310008B01 [Mus mus... 206 5e-52 G

gi|34811715|pdb|1HJ9|A Chain A, Atomic Resolution Structure... 206 5e-52 S

gi|5441855|dbj|BAA82363.1| trypsinogen 2 [Paralichthys oliv... 206 5e-52

gi|12843871|dbj|BAB26143.1| unnamed protein product [Mus mu... 206 5e-52 G

gi|56611170|gb|AAH87830.1| Hypothetical LOC496697 [Xenopus ... 206 6e-52 G

gi|60599777|gb|AAT11803.2| pancreatic trypsinogen [Struthio... 206 6e-52

gi|11244763|gb|AAG33358.1| stratum corneum trypsin-like ser... 206 6e-52 G

gi|2118087|pir||S55067 trypsin (EC 3.4.21.4) I precursor, p... 206 6e-52

gi|2499863|sp|Q90628|TRY2_CHICK Trypsin I-P38 precursor >gi... 206 6e-52 G

gi|51247093|pdb|1H9I|E Chain E, Complex Of Eeti-Ii Mutant W... 206 6e-52 S

gi|2392803|pdb|5PTP| Structure Of Hydrolase (Serine Protei... 206 6e-52 S

gi|33126535|gb|AAL14243.1| protease serine 4 isoform B [Hom... 205 8e-52

gi|18777665|ref|NP_036002.1| kallikrein 7 [Mus musculus] >g... 205 8e-52 G

gi|93017|pir||A27207 tissue kallikrein (EC 3.4.21.35), pros... 205 8e-52

gi|3318722|pdb|1AN1|E Chain E, Leech-Derived Tryptase Inhib... 205 8e-52 S

gi|31541863|ref|NP_075822.2| RIKEN cDNA 2210010C04 [Mus mus... 205 1e-51 G

gi|51593533|gb|AAH78492.1| MGC85264 protein [Xenopus laevis] 205 1e-51 G

gi|476488|pir||KQPG tissue kallikrein (EC 3.4.21.35), pancr... 205 1e-51

gi|58257845|gb|AAW69364.1| try13 [Macaca mulatta] 205 1e-51

gi|56606017|ref|NP_001008416.1| kallikrein 1 [Bos taurus] >... 204 2e-51 G

gi|20141454|sp|P00752|KLK_PIG Glandular kallikrein precurso... 204 2e-51

gi|34856015|ref|XP_214932.2| similar to GLANDULAR KALLIKREI... 204 2e-51 G

gi|27731319|ref|XP_218649.1| similar to thymopsin [Rattus n... 203 4e-51 G

gi|56611173|gb|AAH87759.1| Hypothetical LOC496640 [Xenopus ... 203 4e-51 G

gi|54038747|gb|AAH84612.1| LOC495211 protein [Xenopus laevis] 203 4e-51 G

gi|30584501|gb|AAP36503.1|	Homo sapiens kallikrein 5 [synth...	202	5e-51	
gi|37183138|gb|AAQ89369.1|	KLK5 [Homo sapiens] >gi|31075483...	202	5e-51	G
gi|112403|pir||A34079	tissue kallikrein (EC 3.4.21.35) P1 p...	202	5e-51	G
gi|21594212|gb|AAH32005.1|	Stratum corneum chymotryptic enz...	202	5e-51	G
gi|41054557|ref|NP_955899.1|	Unknown (protein for MGC:66382...	202	5e-51	G
gi|57162224|emb|CAI39655.1|	OTTHUMP00000045395 [Homo sapien...	202	9e-51	
gi|55741639|ref|NP_001003262.1|	kallikrein 1, renal/pancrea...	202	9e-51	G
gi|55662968|emb|CAH69873.1|	protease, serine, 3 (mesotrypsi...	202	9e-51	G
gi|41350549|gb|AAS00515.1|	trypsin [Oreochromis niloticus]	202	9e-51	
gi|55649803|ref|XP_524356.1|	PREDICTED: similar to Kallikre...	201	1e-50	G
gi|2564751|gb|AAC13322.1|	mesotrypsinogen [Homo sapiens] >g...	201	1e-50	G
gi|20988417|gb|AAH30238.1|	Unknown (protein for IMAGE:45379...	201	1e-50	G
gi|1064991|pdb|1TRN|B	Chain B, Trypsin (E.C.3.4.21.4) Compl...	201	1e-50	S
gi|6066378|emb|CAB58178.1|	trypsinogen IV a-form [Homo sapi...	201	1e-50	G
gi|423134|pir||S33496	trypsin (EC 3.4.21.4) IV form a - hum...	201	1e-50	G
gi|30584977|gb|AAP36761.1|	Homo sapiens kallikrein 2, prost...	201	2e-50	
gi|30582139|gb|AAP35296.1|	kallikrein 2, prostatic [Homo sa...	201	2e-50	G
gi|422723|pir||S33772	tissue kallikrein (EC 3.4.21.35) prec...	201	2e-50	
gi|46402490|ref|NP_571783.1|	trypsin [Danio rerio] >gi|2746...	201	2e-50	G
gi|58257846|gb|AAW69365.1|	try12 [Macaca mulatta]	201	2e-50	
gi|41350551|gb|AAS00516.1|	trypsin [Oreochromis aureus]	201	2e-50	
gi|27573671|pdb|1J17|T	Chain T, Factor Xa Specific Inhibito...	201	2e-50	S
gi|5441853|dbj|BAA82362.1|	trypsinogen 1 [Paralichthys oliv...	201	2e-50	
gi|9665236|ref|NP_062544.1|	kallikrein 12 isoform 1 [Homo s...	201	2e-50	G
gi|52345790|ref|NP_001004941.1|	MGC89184 protein [Xenopus t...	200	3e-50	G
gi|13516891|dbj|BAB40329.1|	trypsinogen [Engraulis japonicus]	200	3e-50	
gi|230765|pdb|2TLD|E	Chain E, Bovine Trypsin (E.C.3.4.21.4)...	200	3e-50	S
gi|29366812|ref|NP_036447.1|	kallikrein 9 [Homo sapiens] >g...	199	4e-50	G
gi|57113723|ref|XP_537938.1|	PREDICTED: similar to KLK15 [C...	199	4e-50	G
gi|32402373|gb|AAP81159.1|	trypsinogen [Pangasius hypophtha...	199	4e-50	
gi|34856017|ref|XP_214931.2|	similar to kallikrein [Rattus ...	199	6e-50	G
gi|559508|emb|CAA57701.1|	trypsin [Paranotothenia magellani...	199	6e-50	
gi|49259459|pdb|1V2M|T	Chain T, Benzamidine In Complex With...	199	6e-50	S
gi|609585|gb|AAA58782.1|	kallikrein	199	6e-50	G
gi|1552516|gb|AAC80208.1|	trypsinogen C [Homo sapiens]	198	1e-49	
gi|51094519|gb|EAL23774.1|	protease, serine, 2 (trypsin 2) ...	198	1e-49	G
gi|55629564|ref|XP_519441.1|	PREDICTED: similar to trypsino...	198	1e-49	G
gi|49259460|pdb|1V2N|T	Chain T, Potent Factor Xa Inhibitor ...	198	1e-49	S
gi|3024066|sp|Q28773|KLK1_PAPHA	Kallikrein 1 precursor (Tis...	198	1e-49	
gi|2136330|pir||I38363	trypsin (EC 3.4.21.4) IV form b prec...	198	1e-49	
gi|3980129|emb|CAA50484.1|	trypsinogen IV b-form [Homo sapi...	198	1e-49	G
gi|51539252|gb|AAU06121.1|	trypsinogen [Takifugu rubripes]	197	2e-49	
gi|4809136|gb|AAD30107.1|	trypsinogen-like serine protease ...	197	2e-49	
gi|971196|gb|AAA75001.1|	trypsinogen	197	2e-49	G
gi|13994131|ref|NP_113711.1|	nerve growth factor, gamma [Ra...	197	2e-49	G
gi|34856011|ref|XP_214947.2|	similar to Glandular kallikrei...	197	2e-49	G
gi|57113389|ref|XP_537905.1|	PREDICTED: similar to trypsin ...	197	2e-49	G
gi|33126583|gb|AAL14244.1|	protease serine 2 isoform B [Hom...	197	2e-49	G
gi|20988034|gb|AAH30260.1|	PRSS2 protein [Homo sapiens]	197	2e-49	G

gi|56611148|gb|AAH87751.1|	Hypothetical LOC496633 [Xenopus ...	197	2e-49	G
gi|3452120|gb|AAC32752.1|	trypsinogen 2 precursor [Pseudopl...	197	2e-49	
gi|51539247|gb|AAU06120.1|	trypsinogen [Takifugu rubripes]	197	3e-49	
gi|49259469|pdb|1V2W|T	Chain T, Trypsin Inhibitor In Comple...	197	3e-49	S
gi|20149993|pdb|1H4W|A	Chain A, Structure Of Human Trypsin ...	197	3e-49	S
gi|223207|prf||0608151A	kallikrein B	197	3e-49	
gi|13516893|dbj|BAB40330.1|	trypsinogen II [Engraulis japon...	196	4e-49	
gi|1399811|gb|AAB57732.1|	pretrypsinogen-like serine protea...	196	4e-49	
gi|58257842|gb|AAW69361.1|	Try4 [Macaca mulatta]	196	4e-49	
gi|49259466|pdb|1V2T|T	Chain T, Trypsin Inhibitor In Comple...	196	4e-49	S
gi|1213631|emb|CAA40068.1|	trypsin [Pleuronectes platessa] ...	196	5e-49	
gi|2102686|gb|AAB57728.1|	preprotrypsin-like protease [Diss...	196	5e-49	
gi|481641|pir||S39048	trypsin (EC 3.4.21.4) X - Atlantic co...	196	5e-49	
gi|49259464|pdb|1V2R|T	Chain T, Trypsin Inhibitor In Comple...	196	5e-49	S
gi|49259463|pdb|1V2Q|T	Chain T, Trypsin Inhibitor In Comple...	196	5e-49	S
gi|42543835|pdb|1UTM|A	Chain A, Trypsin Specificity As Eluc...	196	5e-49	S
gi|547788|sp|P00758|KLK1_RAT	Glandular kallikrein, pancreat...	196	6e-49	G
gi|57037493|ref|XP_541470.1|	PREDICTED: similar to enamel m...	196	6e-49	G
gi|49259462|pdb|1V2P|T	Chain T, Trypsin Inhibitor In Comple...	196	6e-49	S
gi|34856013|ref|XP_214939.2|	similar to kallikrein [Rattus ...	195	8e-49	G
gi|40647097|gb|AAR88364.1|	pretrypsinogen [Tautogolabrus ad...	195	8e-49	
gi|58257844|gb|AAW69363.1|	try10 [Macaca mulatta]	195	8e-49	
gi|3452117|gb|AAC32751.1|	trypsinogen 1 precursor [Pseudopl...	195	8e-49	
gi|609583|gb|AAA58781.1|	kallikrein	195	8e-49	G
gi|1334753|emb|CAA54215.1|	trypsinogen X [Gadus morhua]	195	1e-48	
gi|58257848|gb|AAW69367.1|	try16 [Macaca mulatta]	195	1e-48	
gi|476825|pir||A44284	tissue kallikrein (EC 3.4.21.35) homo...	195	1e-48	G
gi|2507250|sp|P16049|TRY1_GADMO	Trypsin I precursor	194	2e-48	
gi|57037489|ref|XP_541469.1|	PREDICTED: similar to kallikre...	194	2e-48	G
gi|33307101|gb|AAQ02911.1|	serine protease KN13 precursor [...	194	2e-48	
gi|33637113|gb|AAQ23713.1|	glandular kallikrein precursor [...	194	2e-48	
gi|1334752|emb|CAA54214.1|	trypsinogen I [Gadus morhua] >gi...	193	4e-48	
gi|64382|emb|CAA49676.1|	trypsin IA [Salmo salar] >gi|42258...	193	4e-48	
gi|64380|emb|CAA49680.1|	trypsin I [Salmo salar] >gi|422581...	193	4e-48	
gi|27731317|ref|XP_218647.1|	similar to Kallikrein 9 precur...	193	4e-48	G
gi|52851385|ref|NP_001005382.1|	glandular kallikrein 12, su...	193	4e-48	G
gi|64386|emb|CAA49678.1|	trypsin II [Salmo salar] >gi|42258...	192	5e-48	
gi|51591907|ref|NP_001003977.1|	glandular kallikrein 11 [Ra...	192	5e-48	G
gi|809221|pdb|1BIT|	The Crystal Structure Of Anionic Salmo...	192	5e-48	S
gi|67558|pir||KQHU	tissue kallikrein (EC 3.4.21.35) precurs...	192	7e-48	G
gi|31980868|ref|NP_034769.4|	kallikrein 6 [Mus musculus] >g...	192	9e-48	G
gi|49256121|gb|AAH72978.1|	MGC82534 protein [Xenopus laevis]	192	9e-48	G
gi|107984|pir||S12764	trypsin (EC 3.4.21.4) III precursor -...	191	1e-47	G
gi|4504875|ref|NP_002248.1|	kallikrein 1 preproprotein [Hom...	191	1e-47	G
gi|24266796|gb|AAN52348.1|	stejnefibrase 1 [Trimeresurus st...	191	1e-47	
gi|9989702|gb|AAG11389.1|	kallikrein [Mus musculus] >gi|918...	191	1e-47	G
gi|51873218|gb|AAU12569.1|	kallikrein precursor [Homo sapiens]	191	2e-47	G
gi|4006842|emb|CAA07055.1|	pallabin2 [Gloydius halys] >gi|1...	191	2e-47	
gi|2293478|gb|AAB65411.1|	trypsinogen A1 [Petromyzon marinu...	191	2e-47	
gi|2367495|gb|AAB69654.1|	trypsinogen a2 [Petromyzon marinus]	191	2e-47	
gi|52851403|ref|NP_032719.1|	nerve growth factor, gamma [Mu...	191	2e-47	G

gi|20160213|gb|AAM11874.1|	kallikrein 1, renal/pancreas/sal...	191	2e-47	G
gi|33307086|gb|AAQ02906.1|	serine protease KN12 precursor [...	190	3e-47	
gi|5001993|gb|AAD37247.1|	chimeric AFGP/trypsinogen-like se...	190	3e-47	
gi|47523236|ref|NP_998967.1|	enamel matrix serine proteinas...	190	3e-47	G
gi|3212609|pdb|1SGF|Z	Chain Z, Crystal Structure Of 7s Ngf:...	189	5e-47	S
gi|55629686|ref|XP_527930.1|	PREDICTED: similar to Trypsin ...	189	5e-47	G
gi|2367501|gb|AAB69657.1|	trypsinogen b2 [Petromyzon marinus]	189	5e-47	
gi|30583345|gb|AAP35917.1|	kallikrein 1, renal/pancreas/sal...	189	6e-47	G
gi|386843|gb|AAA59201.1|	kallikrein	189	8e-47	G
gi|67553|pir||TRDFS	trypsin (EC 3.4.21.4) precursor - spiny...	189	8e-47	
gi|47479455|gb|AAH69325.1|	Kallikrein 4, preproprotein [Hom...	188	1e-46	G
gi|4006844|emb|CAA04612.1|	pallabin [Gloydius halys] >gi|13...	188	1e-46	
gi|1334246|emb|CAA25930.1|	NGF-gamma [Mus musculus]	188	1e-46	
gi|26006097|dbj|BAC41392.1|	anionic trypsin [Oncorhynchus k...	188	1e-46	
gi|4883930|gb|AAD31711.1|	chimeric antifreeze glycoprotein-...	188	1e-46	
gi|4512032|gb|AAD21581.1|	serine protease prostase [Homo sa...	187	2e-46	G
gi|6980535|pdb|2STB|E	Chain E, Anionic Salmon Trypsin In Co...	187	2e-46	S
gi|6010462|gb|AAF01139.1|	stratum corneum chymotryptic enzy...	187	2e-46	G
gi|2367499|gb|AAB69656.1|	trypsinogen B1 [Petromyzon marinus]	187	2e-46	
gi|28875780|ref|NP_034770.1|	kallikrein 11 [Mus musculus] >...	187	3e-46	G
gi|9910516|ref|NP_064312.1|	kallikrein 4 (prostase, enamel ...	187	3e-46	G
gi|13959656|sp|Q9PT41|VSP1_VIPLE	Factor V activating enzyme...	186	4e-46	
gi|18158713|pdb|1HJ8|A	Chain A, 1.00 Aa Trypsin From Atlant...	186	4e-46	S
gi|226064|prf||1409287A	urinary prokallikrein	186	5e-46	
gi|8659568|ref|NP_034775.1|	kallikrein 1 [Mus musculus] >gi...	186	5e-46	G
gi|12002224|gb|AAG43246.1|	enamel matrix serine proteinase ...	186	5e-46	G
gi|515295|pdb|2TBS|	Trypsin (E.C.3.4.21.4) Complexed With ...	186	5e-46	S
gi|223665|prf||0906268A	kallikrein	186	5e-46	
gi|57037481|ref|XP_541467.1|	PREDICTED: similar to kallikre...	186	7e-46	G
gi|24266802|gb|AAN52350.1|	venom serine protease 5 [Trimere...	186	7e-46	
gi|20520629|emb|CAD30563.1|	trypsinogen Y precursor [Gadus ...	186	7e-46	
gi|60593495|pdb|1SPJ|A	Chain A, Structure Of Mature Human T...	185	9e-46	S
gi|3915685|sp|P05620|VSP1_TRIFL	Flavoxobin precursor >gi|21...	185	9e-46	
gi|27573862|pdb|1MBQ|A	Chain A, Anionic Trypsin From Pacifi...	185	1e-45	S
gi|6815045|dbj|BAA82364.2|	trypsinogen 3 [Paralichthys oliv...	185	1e-45	
gi|21426851|ref|NP_034246.1|	kallikrein 9 [Mus musculus] >g...	184	1e-45	G
gi|742152|prf||2009261A	kallidinogenase	184	1e-45	
gi|55650315|ref|XP_524486.1|	PREDICTED: similar to kallikre...	184	1e-45	G
gi|2118085|pir||JC4803	venombin A (EC 3.4.21.74) precursor ...	184	1e-45	
gi|9230643|gb|AAF85937.1|	enamel matrix serine proteinase 1...	184	1e-45	G
gi|26354462|dbj|BAC40859.1|	unnamed protein product [Mus mu...	184	1e-45	G
gi|32329782|emb|CAD86932.1|	proaggregant serine proteinase ...	184	2e-45	
gi|19032293|dbj|BAB85634.1|	trypsinogen [Anguilla japonica]	183	3e-45	
gi|1373148|gb|AAB02196.1|	trypsinogen I	183	4e-45	
gi|51871599|ref|NP_001004101.1|	kallikrein 4 [Rattus norveg...	182	6e-45	G
gi|21309888|gb|AAM46086.1|	thrombin-like enzyme [Gloydius u...	182	6e-45	
gi|55527|emb|CAA35232.1|	pre-pro-protein for kallikrein [Ma...	181	1e-44	
gi|38085510|ref|XP_145260.2|	similar to Trypsin V-A precurs...	181	1e-44	G
gi|8567985|gb|AAF76378.1|	thrombin-like protein DAV-PA prec...	181	1e-44	
gi|4102926|gb|AAD01624.1|	plasminogen activator precursor [...	181	2e-44	
gi|64384|emb|CAA49677.1|	trypsin IB [Salmo salar]	181	2e-44	

gi|7949064|ref|NP_032482.1| kallikrein 5 [Mus musculus] >gi...	181	2e-44	G
gi|39841069|ref|NP_082936.1| kallikrein 9 homolog [Mus musc...	180	3e-44	G
gi|3318901|pdb|1FXY|A Chain A, Coagulation Factor Xa-Trypsi...	180	3e-44	S
gi|602604|emb|CAA58225.1| mucofirase 5 [Protobothrops mucro...	180	4e-44	
gi|311844|emb|CAA51957.1| prostate specific antigen [Macaca...	179	5e-44	
gi|24266793|gb|AAN52347.1| stejnobin [Trimeresurus stejnegeri]	179	5e-44	
gi|32396014|gb|AAP42416.1| serine protease [Bothrops jarara...	179	5e-44	
gi|24637205|gb|AAN63607.1| kallikrein 5 variant [Homo sapie...	179	6e-44	G
gi|602600|emb|CAA58223.1| mucofirase 3 [Protobothrops mucro...	179	6e-44	
gi|6981670|ref|NP_036809.1| tonin [Rattus norvegicus] >gi|6...	179	8e-44	G
gi|23956056|ref|NP_034772.1| kallikrein 21 [Mus musculus] >...	179	8e-44	G
gi|33307047|gb|AAQ02893.1| serine protease KN4 precursor [T...	179	8e-44	
gi|3552036|gb|AAC34898.1| pallase [Gloydius halys]	179	8e-44	
gi|11036673|gb|AAG27253.1| serpentokallikrein-2 [Protobothr...	179	8e-44	
gi|52693913|ref|NP_034244.1| kallikrein 22 [Mus musculus] >...	178	1e-43	G
gi|387167|gb|AAA37682.1| epidermal growth factor binding pr...	178	1e-43	G
gi|3212607|pdb|1SGF|X Chain X, Crystal Structure Of 7s Ngf:...	178	1e-43	S
gi|12313877|ref|NP_064664.1| kallikrein 27 [Mus musculus] >...	177	2e-43	G
gi|52551331|gb|AAU84664.1| trypsin [Oreochromis niloticus]	177	2e-43	
gi|49781153|gb|AAT68459.1| prostate specific antigen precur...	177	2e-43	
gi|20563016|dbj|BAB92021.1| neuropsin [Mus musculus]	177	2e-43	G
gi|52551333|gb|AAU84665.1| trypsin [Oreochromis aureus]	177	2e-43	
gi|8393675|ref|NP_034773.1| kallikrein 24 [Mus musculus] >g...	177	2e-43	G
gi|602598|emb|CAA58222.1| mucofirase 2 [Protobothrops mucro...	177	2e-43	
gi|189524|gb|AAA59995.1| prostate specific antigen precursor	177	3e-43	G
gi|54696586|gb|AAV38665.1| kallikrein 3, (prostate specific...	177	3e-43	G
gi|6691473|dbj|BAA89310.1| protease A [Bothrops jararaca] >...	177	3e-43	
gi|951152|gb|AAB01070.1| preprotrimubin	177	3e-43	
gi|22208984|ref|NP_665895.1| kallikrein 10 precursor [Homo ...	176	4e-43	G
gi|602602|emb|CAA58224.1| mucofirase 4 [Protobothrops mucro...	176	4e-43	
gi|13959638|sp|Q9DF66|VSP3_TRIJE Venom serine proteinase 3 ...	176	4e-43	
gi|464965|sp|P35034|TRYP_PLEPL Trypsin precursor >gi|345579...	176	4e-43	
gi|86006|pir||A32121 snake venom factor V activator (EC 3.4...	176	5e-43	
gi|2118079|pir||I55608 complement factor D (EC 3.4.21.46) p...	176	5e-43	
gi|225915|prf||1403294A gamma seminoprotein	176	5e-43	
gi|818030|emb|CAA27247.1| kallikrein [Rattus norvegicus]	176	5e-43	G
gi|6693854|gb|AAF25008.1| salmonase [Gloydius halys brevica...	176	5e-43	
gi|4102924|gb|AAD01623.1| serine protease; Haly 2 [Gloydius...	176	5e-43	
gi|602596|emb|CAA58221.1| mucofirase 1 [Protobothrops mucro...	176	7e-43	
gi|8659572|ref|NP_035045.1| nerve growth factor, alpha [Mus...	176	7e-43	G
gi|21961233|gb|AAH34518.1| Nerve growth factor, alpha [Mus ...	176	7e-43	G
gi|33307053|gb|AAQ02895.1| serine protease KN6 precursor [T...	176	7e-43	
gi|230371|pdb|1TON| Tonin (E.C. Number Not Assigned)	175	9e-43	S
gi|6706013|emb|CAB65936.1| beta-fibrinogenase [Agkistrodon ...	175	9e-43	
gi|33307092|gb|AAQ02908.1| serine protease KN14 precursor [...	175	9e-43	
gi|13959639|sp|Q9DF67|VSP2_TRIJE Venom serine proteinase 2 ...	175	9e-43	
gi|47131125|dbj|BAD18893.1| blarina toxin [Blarina brevicauda]	175	9e-43	
gi|54696292|gb|AAV38518.1| kallikrein 10 [synthetic construct]	175	1e-42	
gi|12803745|gb|AAH02710.1| Kallikrein 10, precursor [Homo s...	175	1e-42	G
gi|511857|gb|AAA60193.1| prostate-specific antigen	175	1e-42	G
gi|33307077|gb|AAQ02903.1| serine protease KN5 precursor [T...	175	1e-42	
gi|3122187|sp|P81176|VSP1_AGKHA Halystase	175	1e-42	
gi|3044080|gb|AAC13280.1| salmobin [Gloydius halys]	174	2e-42	

gi|34862337|ref|XP_343170.1|	adipsin [Rattus norvegicus]	174	2e-42	G
gi|59956916|dbj|BAD89852.1|	kallikrein2 [Blarina brevicauda]	174	2e-42	
gi|59956914|dbj|BAD89851.1|	kallikrein1 [Blarina brevicauda]	174	2e-42	
gi|13959618|sp|O13060|VSPA_TRIGA	Venom serine proteinase 2A...	174	2e-42	
gi|762984|emb|CAA25932.1|	nerve growth factor alpha-subunit...	174	2e-42	G
gi|19526892|ref|NP_598473.1|	kallikrein 10 [Mus musculus] >...	174	3e-42	G
gi|33307095|gb|AAQ02909.1|	serine protease CL4 precursor [T...	174	3e-42	
gi|51870931|ref|NP_001004100.1|	kallikrein 10 [Rattus norve...	173	3e-42	G
gi|38146946|gb|AAR11859.1|	thrombin-like enzyme [Gloydius s...	173	3e-42	
gi|33307089|gb|AAQ02907.1|	serine protease KN7 precursor [T...	173	3e-42	
gi|29468347|gb|AAO85513.1|	protein C activator [synthetic c...	172	6e-42	
gi|2407645|gb|AAB70575.1|	capillary permeability-increasing...	172	6e-42	
gi|7435610|pir||JE0236	tissue kallikrein (EC 3.4.21.35) - m...	172	6e-42	G
gi|6753734|ref|NP_034245.1|	kallikrein 13 [Mus musculus] >g...	172	7e-42	G
gi|104457|pir||A41456	venombin A (EC 3.4.21.74) [validated]...	172	7e-42	
gi|11036675|gb|AAG27254.1|	serpentokallikrein-1 [Protobothr...	172	7e-42	
gi|49258367|pdb|1OP2|A	Chain A, Crystal Structure Of Aav-Sp...	172	7e-42	S
gi|1633237|pdb|1DST|	Mutant Of Factor D With Enhanced Cata...	172	7e-42	S
gi|62464|emb|CAA31240.1|	batroxobin [Bothrops atrox] >gi|86...	172	1e-41	
gi|29293675|gb|AAO67553.1|	thrombin-like enzyme precursor P...	172	1e-41	
gi|56789072|gb|AAH88011.1|	Hypothetical LOC496746 [Xenopus ...	172	1e-41	G
gi|11378386|pir||JG0169	venombin A (EC 3.4.21.74) [validate...	172	1e-41	
gi|4378029|gb|AAD19350.1|	thrombin-like defibrase 1 [Deinag...	172	1e-41	
gi|86007|pir||B32121	snake venom factor V activator (EC 3.4...	171	1e-41	
gi|24266790|gb|AAN52346.1|	venom serine protease 1 [Trimere...	171	2e-41	
gi|280699|pir||A60468	venombin A (EC 3.4.21.74) - southern ...	171	2e-41	
gi|56566179|gb|AAV98367.1|	thrombin-like protein precursor ...	171	2e-41	
gi|18072835|emb|CAC80981.1|	putative serine proteinase [Cro...	171	2e-41	
gi|3242120|emb|CAA07315.1|	trypsin [Dicentrarchus labrax]	170	3e-41	
gi|33307059|gb|AAQ02897.1|	serine protease KN2 precursor [T...	170	3e-41	
gi|13959619|sp|O13061|VSPB_TRIGA	Venom serine proteinase 2B...	170	3e-41	
gi|49258366|pdb|1OP0|A	Chain A, Crystal Structure Of Aav-Sp...	170	3e-41	S
gi|31322299|gb|AAP20638.1|	thrombin-like enzyme defibrase [...	170	4e-41	
gi|33307068|gb|AAQ02900.1|	serine protease KN11 precursor [...	170	4e-41	
gi|3668352|gb|AAC61838.1|	salmobin [Gloydius halys]	170	4e-41	
gi|211031|gb|AAA48553.1|	batroxobin	170	4e-41	
gi|223879|prf||1003216A	tonin	170	4e-41	
gi|14646873|gb|AAK71702.1|	ARM1 [Homo sapiens]	169	5e-41	G
gi|28461159|ref|NP_786935.1|	kallikrein, submaxillary gland...	169	5e-41	G
gi|57037477|ref|XP_541466.1|	PREDICTED: similar to kallikre...	169	5e-41	G
gi|33307080|gb|AAQ02904.1|	serine protease CL5 precursor [T...	169	6e-41	
gi|33307050|gb|AAQ02894.1|	serine protease KN1 precursor [T...	169	8e-41	
gi|54650274|dbj|BAD66927.1|	hypothetical protein [Bothrops ...	169	8e-41	
gi|14646869|gb|AAK71700.1|	ARM1 [Homo sapiens]	168	1e-40	G
gi|33307062|gb|AAQ02898.1|	serine protease CL1 precursor [T...	168	1e-40	
gi|22417221|gb|AAM96700.1|	serine beta-fibrinogenase precur...	167	2e-40	
gi|6562944|emb|CAB62591.1|	serine proteinase, homolog [Macr...	167	2e-40	
gi|33307056|gb|AAQ02896.1|	serine protease KN9 precursor [T...	167	2e-40	
gi|13959620|sp|O13062|VSPC_TRIGA	Venom serine proteinase 2C...	167	2e-40	
gi|6754460|ref|NP_034774.1|	kallikrein 26 [Mus musculus] >g...	167	2e-40	G
gi|2624768|pdb|1AO5|B	Chain B, Mouse Glandular Kallikrein-1...	167	2e-40	S
gi|13959621|sp|O13063|VSP3_TRIGA	Venom serine proteinase 3 ...	167	3e-40	
gi|20069139|gb|AAM09695.1|	serine proteinase precursor [Bot...	166	4e-40	
gi|33307071|gb|AAQ02901.1|	serine protease CL3 precursor [T...	166	4e-40	
gi|18652951|gb|AAL77226.1|	serine protease catroxase I prec...	166	5e-40	

gi|8567983|gb|AAF76377.1|	thrombin-like protein acutobin pr...	166	5e-40	
gi|885976|gb|AAC59686.1|	venom plasminogen activator precur...	166	7e-40	
gi|17933276|gb|AAL48222.1|	thrombin-like enzyme ussurase [G...	166	7e-40	
gi|6093643|sp|P81824|VSP1_BOTJA	Platelet-aggregating protei...	166	7e-40	
gi|35505509|gb|AAH57807.1|	Complement factor D, preproprote...	165	9e-40	G
gi|41055921|ref|NP_956439.1|	similar to adrenal secretory s...	165	9e-40	G
gi|17933274|gb|AAL48221.1|	thrombin-like enzyme ussurin [Gl...	165	1e-39	
gi|8567987|gb|AAF76379.1|	thrombin-like protein DAV-KN prec...	165	1e-39	
gi|57791760|gb|AAW56633.1|	thrombin-like enzyme 2 [Deinagki...	165	1e-39	
gi|479945|pir||S35689	venombin A (EC 3.4.21.74) [validated]...	164	2e-39	
gi|13959617|sp|O13059|VSP1_TRIGA	Venom serine proteinase 1 ...	164	2e-39	
gi|3915626|sp|P00746|CFAD_HUMAN	Complement factor D precurs...	164	2e-39	G
gi|33307098|gb|AAQ02910.1|	serine protease PA precursor [Tr...	164	2e-39	
gi|33307065|gb|AAQ02899.1|	serine protease KN10 precursor [...	164	2e-39	
gi|34784418|gb|AAH57674.1|	Tmprss6 protein [Mus musculus]	164	3e-39	G
gi|34856170|ref|XP_218564.2|	similar to kallikrein 5 prepro...	164	3e-39	G
gi|31980537|gb|AAP69827.1|	matriptase-2 [Mus musculus] >gi|...	164	3e-39	G
gi|13095440|gb|AAK12273.1|	thrombin-like enzyme precursor [...	163	3e-39	
gi|54038701|gb|AAH84389.1|	LOC495174 protein [Xenopus laevis]	163	3e-39	G
gi|13959615|sp|O13057|VSP2_TRIFL	Venom serine proteinase 2 ...	163	3e-39	
gi|2134238|pir||S65621	venombin AB (EC 3.4.21.55) [validate...	163	5e-39	
gi|627292|pir||A54361	venombin A (EC 3.4.21.74) [validated]...	163	5e-39	
gi|7705572|ref|NP_032483.1|	kallikrein 8 [Mus musculus] >gi...	163	5e-39	G
gi|24266799|gb|AAN52349.1|	stejnefibrase 2 [Trimeresurus st...	163	5e-39	
gi|55249559|gb|AAH40146.1|	DF protein [Homo sapiens]	163	5e-39	G
gi|33637115|gb|AAQ23714.1|	glandular kallikrein precursor [...	163	5e-39	
gi|56789422|gb|AAH88038.1|	LOC496767 protein [Xenopus tropi...	163	5e-39	G
gi|30048431|gb|AAH51001.1|	DF protein [Homo sapiens]	163	5e-39	G
gi|21961485|gb|AAH34529.1|	DF protein [Homo sapiens] >gi|67...	163	5e-39	G S
gi|5360907|emb|CAB46431.1|	acubin [Deinagkistrodon acutus]	162	6e-39	
gi|14646871|gb|AAK71701.1|	ARM1 [Homo sapiens]	162	6e-39	G
gi|33307074|gb|AAQ02902.1|	serine protease KN3 precursor [T...	162	6e-39	
gi|228276|prf||1802275A	pro-renin-converting enzyme	162	6e-39	
gi|49168634|emb|CAG38812.1|	DF [Homo sapiens]	162	8e-39	G
gi|27229129|ref|NP_082178.1|	type II transmembrane serine p...	162	8e-39	G
gi|18652953|gb|AAL77227.1|	serine protease catroxase II pre...	162	8e-39	
gi|33307104|gb|AAQ02912.1|	serine protease KN8 precursor [T...	162	8e-39	
gi|9988779|gb|AAG10788.1|	serine proteinase 1 precursor [Tr...	162	8e-39	
gi|5822045|pdb|1DIC|A	Chain A, Structure Of 3,4-Dichloroiso...	162	8e-39	S
gi|31322297|gb|AAP20637.1|	thrombin-like enzyme defibrase [...	162	1e-38	
gi|54650276|dbj|BAD66928.1|	hypothetical protein [Bothrops ...	161	1e-38	
gi|32469800|sp|P82981|VSP2_AGKCO	Contortrixobin	161	1e-38	
gi|673431|emb|CAA28379.1|	precursor adipsin [Mus musculus]	161	1e-38	G
gi|7304867|ref|NP_038487.1|	adipsin [Mus musculus] >gi|6758...	161	2e-38	G
gi|13959616|sp|O13058|VSP3_TRIFL	Venom serine proteinase 3 ...	161	2e-38	
gi|67580|pir||DBHU	complement factor D (EC 3.4.21.46) precu...	160	2e-38	
gi|915533|gb|AAA73627.1|	putative preproadipsin [Sus scrofa...	160	2e-38	
gi|47197455|emb|CAF93307.1|	unnamed protein product [Tetrao...	160	2e-38	
gi|21618854|gb|AAH31798.1|	Kallikrein 8 [Mus musculus]	160	3e-38	G
gi|54650278|dbj|BAD66929.1|	hypothetical protein [Bothrops ...	160	3e-38	
gi|22417112|gb|AAM96674.1|	serine alpha-fibrinogenase precu...	160	4e-38	
gi|9581530|emb|CAC00530.1|	acubin2 [Deinagkistrodon acutus]	160	4e-38	
gi|1334162|emb|CAA35231.1|	kallikrein [Mastomys natalensis]...	159	5e-38	

gi|7019443|ref|NP_032480.1|	kallikrein 16 [Mus musculus] >g...	159	5e-38	G
gi|50796084|ref|XP_423832.1|	PREDICTED: similar to MGC69002...	159	5e-38	G
gi|38570060|gb|AAR24534.1|	serine protease 1 [Bitis gabonica]	159	7e-38	
gi|57791683|gb|AAW56609.1|	thrombin-like protein 3 [Deinagk...	159	7e-38	
gi|178626|gb|AAA35527.1|	adipsin/complement factor D	158	1e-37	G
gi|8567989|gb|AAF76380.1|	thrombin-like protein precursor [...	158	1e-37	
gi|39794386|gb|AAH64208.1|	Hypothetical protein MGC76105 [X...	158	1e-37	G
gi|5821882|pdb|1BQY|B	Chain B, Plasminogen Activator (Tsv-P...	158	1e-37	S
gi|45383251|ref|NP_989788.1|	granzyme A [Gallus gallus] >gi...	157	2e-37	G
gi|50746751|ref|XP_420637.1|	PREDICTED: similar to neurotry...	157	2e-37	G
gi|480383|pir||S36783	venombin A (EC 3.4.21.74) 2 precursor...	157	2e-37	
gi|57869385|gb|AAW57544.1|	neurotrypsin [Saguinus labiatus]	157	2e-37	
gi|15042973|gb|AAK52506.2|	venom thrombin-like enzyme [Dein...	157	3e-37	
gi|52354657|gb|AAH82912.1|	LOC494791 protein [Xenopus laevis]	157	3e-37	G
gi|57791681|gb|AAW56608.1|	thrombin-like protein 1 [Deinagk...	157	3e-37	
gi|37181921|gb|AAQ88764.1|	PVAE354 [Homo sapiens]	156	4e-37	G
gi|13959622|sp|O13069|VSP2_BOTJA	Kinin-releasing and fibrin...	156	6e-37	
gi|57092775|ref|XP_531743.1|	PREDICTED: similar to transmem...	155	7e-37	G
gi|33307083|gb|AAQ02905.1|	serine protease CL2 precursor [T...	155	9e-37	
gi|24158620|pdb|1GVZ|A	Chain A, Prostate Specific Antigen (...	155	9e-37	S
gi|23428417|gb|AAL16414.1|	type II transmembrane serine pro...	155	1e-36	G
gi|56417706|emb|CAI19335.1|	OTTHUMP00000028798 [Homo sapiens]	155	1e-36	G
gi|23477115|emb|CAC85953.1|	matriptase-2 [Homo sapiens]	155	1e-36	G
gi|57869340|gb|AAW57541.1|	neurotrypsin [Hylobates leucogenys]	154	2e-36	
gi|57869310|gb|AAW57539.1|	neurotrypsin [Gorilla gorilla]	154	2e-36	
gi|47228305|emb|CAG07700.1|	unnamed protein product [Tetrao...	154	2e-36	
gi|56693556|gb|AAW22597.1|	neurotrypsin [Hylobates hoolock]	154	2e-36	
gi|47229070|emb|CAG03822.1|	unnamed protein product [Tetrao...	154	2e-36	

Alignments

Get selected sequences | Select all | Deselect all

```
>gi|21411424|gb|AAH31119.1| G Prss18 protein [Mus musculus]
 gi|14141579|dbj|BAB55605.1| G neurosin [Mus musculus]
          Length = 253

 Score =  544 bits (1401), Expect = e-154
 Identities = 253/253 (100%), Positives = 253/253 (100%)

Query: 1   MPMKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID 60
            MPMKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID
Sbjct: 1   MPMKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID 60

Query: 61  PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
            PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK
Sbjct: 61  PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120

Query: 121 NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYP 180
            NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYP
Sbjct: 121 NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYP 180
```

```
Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
           GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH
Sbjct: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240

Query: 241 IRWIQNILRNKWL 253
           IRWIQNILRNKWL
Sbjct: 241 IRWIQNILRNKWL 253
```

>gi|6755180|ref|NP_035307.1| protease, serine, 18 [Mus musculus]
gi|4220546|emb|CAA77269.1| serine protease (BSSP) [Mus musculus]
gi|3241912|dbj|BAA28895.1| serine protease (BSP) [Mus musculus]
gi|5913973|dbj|BAA84544.1| brain serine protease [Mus musculus]
Length = 246

Score = 530 bits (1365), Expect = e-149
Identities = 246/246 (100%), Positives = 246/246 (100%)

```
Query: 8   MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
           MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA
Sbjct: 1   MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 60

Query: 68  AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
           AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK
Sbjct: 61  AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 120

Query: 128 KIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 187
           KIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSM
Sbjct: 121 KIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 180

Query: 188 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
           VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI
Sbjct: 181 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 240

Query: 248 LRNKWL 253
           LRNKWL
Sbjct: 241 LRNKWL 246
```

>gi|9506997|ref|NP_062048.1| kallikrein 6 [Rattus norvegicus]
gi|2853366|gb|AAC02300.1| myelencephalon specific protease [Rattus norvegicus]
Length = 251

Score = 492 bits (1266), Expect = e-138
Identities = 223/251 (88%), Positives = 241/251 (96%)

```
Query: 1   MPMKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID 60
           MP KMLT+K LALCL+LAKSAWSE+Q+KVVHGGPCLK+SHPFQAALYTSGHLLCGGVL+
Sbjct: 1   MPTKMLTVKTLALCLILAKSAWSEDQDKVVHGGPCLKNSHPFQAALYTSGHLLCGGVLVG 60

Query: 61  PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
           PQWVLTAAHCKKPNL+V LGKHNLRQTETFQRQISVDRTIVHPRYNP+THDNDIMMVHLK
Sbjct: 61  PQWVLTAAHCKKPNLEVYLGKHNLRQTETFQRQISVDRTIVHPRYNPQTHDNDIMMVHLK 120

Query: 121 NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYP 180
            PVKFS++IQPLPLK DCSE+NP+CQILGWGKMENG+FPDTIQCADV LV RE+CERAYP
```

```
Sbjct: 121 RPVKFSQRIQPLPLKKDCSEKNPDCQILGWGKMENGEFPDTIQCADVQLVSREECERAYP 180

Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
           GKIT+SMVCAGD +EGNDSCQGDSGGPLVCGG LRG+VSWGDMPCGSKEKPGVYTDVCTH
Sbjct: 181 GKITRSMVCAGDKREGNDSCQGDSGGPLVCGGHLRGIVSWGDMPCGSKEKPGVYTDVCTH 240

Query: 241 IRWIQNILRNK 251
           IRWIQNI+RNK
Sbjct: 241 IRWIQNIIRNK 251
```

>gi|57036286|ref|XP_533605.1| G PREDICTED: similar to Kallikrein 6 precursor (Prote
(Neurosin) (Zyme) (SP59) [Canis familiaris]
Length = 528

```
 Score =  367 bits (943), Expect = e-100
 Identities = 167/238 (70%), Positives = 194/238 (81%)

Query: 12  ALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCK 71
           +L   L  SAW+EEQ KV+HGGPC + SHP+QAALYTSGHLLCGGVLI P WVLTAAHCK
Sbjct: 289 SLTQTLPFSAWAEEQNKVLHGGPCEQTSHPYQAALYTSGHLLCGGVLIHPLWVLTAAHCK 348

Query: 72  KPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQP 131
           KPNLQV LGKHNL+Q E+FQ Q SV R + HP YN  THD DIM++ L   P KFS++IQP
Sbjct: 349 KPNLQVYLGKHNLQQRESFQEQSSVVRAVAHPGYNAATHDQDIMLLRLARPAKFSERIQP 408

Query: 132 LPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAG 191
           L L+ DCS  + +C ILGWGK  +GDFP+TIQCA +HLVPRE+CERAYP +ITQ+MVCAG
Sbjct: 409 LSLEQDCSANHSSCHILGWGKTADGDFPNTIQCAYIHLVPREECERAYPSQITQNMVCAG 468

Query: 192 DMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
           D K G DSCQGDSGGPLVCG RLRGLVSWG++PCGSKEKPGVYTDVC +  WI+  ++
Sbjct: 469 DEKYGKDSCQGDSGGPLVCGDRLRGLVSWGNVPCGSKEKPGVYTDVCRYGHWIRKTIQ 526


 Score =  192 bits (489), Expect = 5e-48
 Identities = 89/214 (41%), Positives = 123/214 (57%), Gaps = 4/214 (1%)

Query: 27  EKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQ 86
           EK++ G PC + SHP+Q AL      L CGGVL++ QWVLTAAHC       V +G   L
Sbjct: 13  EKIIEGVPCTRGSHPWQVALLKGTQLHCGGVLLNEQWVLTAAHCMMSEYNVHMGSDQLSD 72

Query: 87  TETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQ 146
                ++I    R+  HP Y+ +TH ND+M+V L     + S +++ + L + C       C
Sbjct: 73  KRA--QKIRATRSFRHPGYSTQTHVNDLMLVKLSKQARLSSRVKKVNLPSRCEPPGTTCT 130

Query: 147 ILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDS 204
           + GWG    + D  FP  + C DV L+   + C++ Y   + +SM+CAG        ++C GDS
Sbjct: 131 VSGWGTTTSPDVTFPSKLMCTDVKLISSQDCKKVYKDLLGKSMLCAGIPNSKTNACNGDS 190

Query: 205 GGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVC 238
           GGPL+C G L+GLVSWG  PCG    PGVYT VC
Sbjct: 191 GGPLMCKGALQGLVSWGTFPCGQPNDPGVYTQVC 224
```

>gi|15930186|gb|AAH15525.1| G KLK6 protein [Homo sapiens]

gi|30582543|gb|AAP35498.1| G kallikrein 6 (neurosin, zyme) [Homo sapiens]
gi|4506155|ref|NP_002765.1| G kallikrein 6 preproprotein [Homo sapiens]
gi|5791636|gb|AAD51475.1| G kallikrein-like serine protease; zyme; protease M; neuro sapiens]
gi|32448678|gb|AAP82448.1| G kallikrein 6 precursor [Homo sapiens]
gi|32448674|gb|AAP82446.1| G kallikrein 6 precursor [Homo sapiens]
gi|1518788|gb|AAB07113.1| G protease M [Homo sapiens]
gi|11244764|gb|AAG33359.1| G protease M [Homo sapiens]
gi|2318115|gb|AAB66483.1| G serine protease [Homo sapiens]
gi|3914480|sp|Q92876|KLK6_HUMAN G Kallikrein 6 precursor (Protease M) (Neurosin) (Zy
gi|1805493|dbj|BAA11306.1| G neurosin [Homo sapiens]
Length = 244

```
 Score =  366 bits (940), Expect = e-100
 Identities = 167/244 (68%), Positives = 194/244 (79%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK L + L L  +AW+EEQ K+VHGGPC K SHP+QAALYTSGHLLCGGVLI P WVLTA
Sbjct: 1    MKKLMVVLSLIAAAWAEEQNKLVHGGPCDKTSHPYQAALYTSGHLLCGGVLIHPLWVLTA 60

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHCKKPNLQV LGKHNLRQ E+ Q Q SV R ++HP Y+  +HD DIM++ L  P K S+
Sbjct: 61   AHCKKPNLQVFLGKHNLRQRESSQEQSSVVRAVIHPDYDAASHDQDIMLLRLARPAKLSE 120

Query: 128  KIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 187
             IQPLPL+ DCS    +C ILGWGK  +GDFPDTIQCA +HLV RE+CE AYPG+ITQ+M
Sbjct: 121  LIQPLPLERDCSANTTSCHILGWGKTADGDFPDTIQCAYIHLVSREECEHAYPGQITQNM 180

Query: 188  VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
            +CAGD K G DSCQGDSGGPLVCG  LRGLVSWG++PCGSKEKPGVYT+VC +  WIQ
Sbjct: 181  LCAGDEKYGKDSCQGDSGGPLVCGDHLRGLVSWGNIPCGSKEKPGVYTNVCRYTNWIQKT 240

Query: 248  LRNK 251
            ++ K
Sbjct: 241  IQAK 244
```

>gi|30585043|gb|AAP36794.1| Homo sapiens kallikrein 6 (neurosin, zyme) [synthetic c
Length = 245

```
 Score =  366 bits (940), Expect = e-100
 Identities = 167/244 (68%), Positives = 194/244 (79%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK L + L L  +AW+EEQ K+VHGGPC K SHP+QAALYTSGHLLCGGVLI P WVLTA
Sbjct: 1    MKKLMVVLSLIAAAWAEEQNKLVHGGPCDKTSHPYQAALYTSGHLLCGGVLIHPLWVLTA 60

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHCKKPNLQV LGKHNLRQ E+ Q Q SV R ++HP Y+  +HD DIM++ L  P K S+
Sbjct: 61   AHCKKPNLQVFLGKHNLRQRESSQEQSSVVRAVIHPDYDAASHDQDIMLLRLARPAKLSE 120

Query: 128  KIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 187
             IQPLPL+ DCS    +C ILGWGK  +GDFPDTIQCA +HLV RE+CE AYPG+ITQ+M
Sbjct: 121  LIQPLPLERDCSANTTSCHILGWGKTADGDFPDTIQCAYIHLVSREECEHAYPGQITQNM 180
```

```
Query: 188 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
           +CAGD K G DSCQGDSGGPLVCG  LRGLVSWG++PCGSKEKPGVYT+VC +  WIQ
Sbjct: 181 LCAGDEKYGKDSCQGDSGGPLVCGDHLRGLVSWGNIPCGSKEKPGVYTNVCRYTNWIQKT 240

Query: 248 LRNK 251
           ++ K
Sbjct: 241 IQAK 244
```

>gi|55233182|gb|AAV48554.1| kallikrein 6 preproprotein [synthetic construct]
Length = 283

Score = 366 bits (940), Expect = e-100
Identities = 167/244 (68%), Positives = 194/244 (79%)

```
Query: 8   MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
           MK L + L L  +AW+EEQ K+VHGGPC K SHP+QAALYTSGHLLCGGVLI P WVLTA
Sbjct: 1   MKKLMVVLSLIAAAWAEEQNKLVHGGPCDKTSHPYQAALYTSGHLLCGGVLIHPLWVLTA 60

Query: 68  AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
           AHCKKPNLQV LGKHNLRQ E+ Q Q SV R ++HP Y+  +HD DIM++ L  P K S+
Sbjct: 61  AHCKKPNLQVFLGKHNLRQRESSQEQSSVVRAVIHPDYDAASHDQDIMLLRLARPAKLSE 120

Query: 128 KIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 187
            IQPLPL+ DCS    +C ILGWGK  +GDFPDTIQCA +HLV RE+CE AYPG+ITQ+M
Sbjct: 121 LIQPLPLERDCSANTTSCHILGWGKTADGDFPDTIQCAYIHLVSREECEHAYPGQITQNM 180

Query: 188 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
           +CAGD K G DSCQGDSGGPLVCG  LRGLVSWG++PCGSKEKPGVYT+VC +  WIQ
Sbjct: 181 LCAGDEKYGKDSCQGDSGGPLVCGDHLRGLVSWGNIPCGSKEKPGVYTNVCRYTNWIQKT 240

Query: 248 LRNK 251
           ++ K
Sbjct: 241 IQAK 244
```

>gi|21465525|pdb|1GVL|A Chain A, Human Prokallikrein 6 (Hk6) PROZYME PROPROTEASE
Proneurosin
Length = 223

Score = 347 bits (891), Expect = 1e-94
Identities = 156/222 (70%), Positives = 181/222 (81%)

```
Query: 28  KVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQT 87
           K+VHGGPC K SHP+QAALYTSGHLLCGGVLI P WVLTAAHCKKPNLQV LGKHNLRQ
Sbjct: 1   KLVHGGPCDKTSHPYQAALYTSGHLLCGGVLIHPLWVLTAAHCKKPNLQVFLGKHNLRQQ 60

Query: 88  ETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQI 147
           E+ Q Q SV R ++HP Y+  +HD DIM++ L  P K S+ IQPLPL+ DCS +  +C I
Sbjct: 61  ESSQEQSSVVRAVIHPDYDAASHDQDIMLLRLARPAKLSELIQPLPLERDCSAQTTSCHI 120

Query: 148 LGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGP 207
           LGWGK  +GDFPDTIQCA +HLV RE+CE AYPG+ITQ+M+CAGD K G DSCQGDSGGP
Sbjct: 121 LGWGKTADGDFPDTIQCAYIHLVSREECEHAYPGQITQNMLCAGDEKYGKDSCQGDSGGP 180

Query: 208 LVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
           LVCG  LRGLVSWG++PCGSKEKPGVYT+VC +  WIQ  ++
```

```
Sbjct: 181 LVCGDHLRGLVSWGNIPCGSKEKPGVYTNVCRYTNWIQKTIQ 222
```

>gi|21466131|pdb|1L06|A S Chain A, Human Kallikrein 6 (Hk6) Active Form With Benzar
          Inhibitor At 1.56 A Resolution
 gi|21465970|pdb|1L2E|A S Chain A, Human Kallikrein 6 (Hk6) Active Form With Benzamid
          Inhibitor
         Length = 223

```
 Score =  346 bits (887), Expect = 4e-94
 Identities = 156/223 (69%), Positives = 180/223 (80%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +VHGGPC K SHP+QAALYTSGHLLCGGVLI P WVLTAAHCKKPNLQV LGKHNLRQ E
Sbjct: 1    LVHGGPCDKTSHPYQAALYTSGHLLCGGVLIHPLWVLTAAHCKKPNLQVFLGKHNLRQRE 60

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
             + Q Q SV R ++HP Y+   +HD DIM++ L   P K S+ IQPLPL+ DCS     +C IL
Sbjct: 61   SSQEQSSVVRAVIHPDYDAASHDQDIMLLRLARPAKLSELIQPLPLERDCSANTTSCHIL 120

Query: 149 GWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPL 208
             GWGK   +GDFPDTIQCA +HLV RE+CE AYPG+ITQ+M+CAGD K G DSCQGDSGGPL
Sbjct: 121  GWGKTADGDFPDTIQCAYIHLVSREECEHAYPGQITQNMLCAGDEKYGKDSCQGDSGGPL 180

Query: 209 VCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRNK 251
             VCG  LRGLVSWG++PCGSKEKPGVYT+VC +  WIQ  ++ K
Sbjct: 181 VCGDHLRGLVSWGNIPCGSKEKPGVYTNVCRYTNWIQKTIQAK 223
```

>gi|37183190|gb|AAQ89395.1| G KLK8 [Homo sapiens]
 gi|6005844|ref|NP_009127.1| G kallikrein 8 isoform 1 preproprotein [Homo sapiens]
 gi|3176387|dbj|BAA28673.1| G neuropsin [Homo sapiens]
 gi|4768607|gb|AAD29574.1| G serine protease ovasin [Homo sapiens]
 gi|5918518|gb|AAD56050.1| serine protease TADG14 [Homo sapiens]
 gi|4588082|gb|AAD25979.1| G serine protease ovasin [Homo sapiens]
 gi|11244766|gb|AAG33361.1| G neuropsin [Homo sapiens]
 gi|6093536|sp|O60259|KLK8_HUMAN G Neuropsin precursor (NP) (Kallikrein 8) (Ovasin) (
          TADG-14) (Tumor-associated differentially expressed
          gene-14 protein) (UNQ283/PRO322)
 gi|5672473|dbj|BAA82665.1| G neuropsin type1 [Homo sapiens]
         Length = 260

```
 Score =  241 bits (614), Expect = 2e-62
 Identities = 112/246 (45%), Positives = 164/246 (66%), Gaps = 10/246 (4%)

Query: 15   LVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC 70
             L+L   AW+      +++KV+ G  C   S P+QAAL+      LLCGGVL+   WVLTAAHC
Sbjct: 15   LLLLGGAWAGHSRAQEDKVLGGHECQPHSQPWQAALFQGQQLLCGGVLVGGNWVLTAAHC 74

Query: 71   KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP---ETHDNDIMMVHLKNPVKFSK 127
             KKP   V LG H+L+  +  +++I V ++I HP YN    E H++D+M++ L++
Sbjct: 75   KKPKYTVRLGDHSLQNKDGPEQEIPVVQSIPHPCYNSSDVEDHNHDLMLLQLRDQASLGS 134

Query: 128  KIQPLPLKNDCSEENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQ 185
             K++P+ L + C++    C + GWG + +   +FPDT+ CA+V + P+++CE AYPG+IT
```

```
Sbjct: 135 KVKPISLADHCTQPGQKCTVSGWGTVTSPRENFPDTLNCAEVKIFPQKKCEDAYPGQITD 194

Query: 186 SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            MVCAG  K G D+CQGDSGGPLVC G L+G+ SWG  PCG  +KPGVYT++C ++ WI+
Sbjct: 195 GMVCAGSSK-GADTCQGDSGGPLVCDGALQGITSWGSDPCGRSDKPGVYTNICRYLDWIK 253

Query: 246 NILRNK 251
            I+ +K
Sbjct: 254 KIIGSK 259
```

>gi|55649729|ref|XP_512847.1| G PREDICTED: similar to kallikrein 8 isoform 1 prepro
protease, serine, 19; neuropsin; ovasin;
tumor-associated differentially expressed gene 14 [Pan
troglodytes]
Length = 505

```
 Score =  241 bits (614), Expect = 2e-62
 Identities = 112/246 (45%), Positives = 164/246 (66%), Gaps = 10/246 (4%)

Query: 15  LVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC 70
           L+L   AW+      +++KV+ G  C   S P+QAAL+     LLCGGVL+    WVLTAAHC
Sbjct: 260 LLLLGGAWAGHSRAQEDKVLGGHECQPHSQPWQAALFQGQQLLCGGVLVGGNWVLTAAHC 319

Query: 71  KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP---ETHDNDIMMVHLKNPVKFSK 127
           KKP   V LG H+L+  +   +++I V ++I HP YN    E H++D+M++ L++
Sbjct: 320 KKPKYTVRLGDHSLQNKDGPEQEIPVVQSIPHPCYNSSDVEDHNHDLMLLQLRDQASLGS 379

Query: 128 KIQPLPLKNDCSEENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQ 185
           K++P+ L + C++     C + GWG + +   +FPDT+ CA+V + P+++CE AYPG+IT
Sbjct: 380 KVKPISLADHCTQPGQKCTVSGWGTVTSPRENFPDTLNCAEVKIFPQKKCEDAYPGQITD 439

Query: 186 SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            MVCAG  K G D+CQGDSGGPLVC G L+G+ SWG  PCG  +KPGVYT++C ++ WI+
Sbjct: 440 GMVCAGSSK-GADTCQGDSGGPLVCDGALQGITSWGSDPCGRSDKPGVYTNICRYLDWIK 498

Query: 246 NILRNK 251
            I+ +K
Sbjct: 499 KIIGSK 504


 Score = 49.3 bits (116), Expect = 1e-04
 Identities = 20/39 (51%), Positives = 26/39 (66%)

Query: 35  CLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKP 73
           C  +S P+QA L+     L CG  LI  +W+LTAAHC+KP
Sbjct: 113 CRPNSQPWQAGLFHLTRLFCGATLISDRWLLTAAHCRKP 151


 Score = 44.3 bits (103), Expect = 0.003
 Identities = 19/62 (30%), Positives = 33/62 (53%), Gaps = 8/62 (12%)

Query: 98  RTIVHPRYNP--------ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILG 149
           R++VHP+Y+            T ++D+M++ L  PV    + + L L   C++     CQ+ G
Sbjct: 31  RSVVHPKYHQGSGPILPRRTDEHDLMLLKLARPVVLGPRARALQLPYRCAQPGDQCQVAG 90

Query: 150 WG 151
```

```
         WG
Sbjct: 91  WG 92


>gi|26454807|gb|AAH40887.1|  Kallikrein 8, isoform 1 preproprotein [Homo sapiens]
          Length = 260

 Score =  240 bits (612), Expect = 3e-62
 Identities = 112/246 (45%), Positives = 164/246 (66%), Gaps = 10/246 (4%)

Query: 15   LVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC 70
            L+L   AW+      +++KV+ G  C   S P+QAAL+     LLCGGVL+    WVLTAAHC
Sbjct: 15   LLLLGGAWAGHSRAQEDKVLGGHECQPHSQPWQAALFQGQQLLCGGVLVGGNWVLTAAHC 74

Query: 71   KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP---ETHDNDIMMVHLKNPVKFSK 127
            KKP    V LG H+L+  +  +++I V ++I HP YN    E H++D+M++ L++
Sbjct: 75   KKPKYTVRLGDHSLQNKDGPEQEIPVVQSIPHPCYNSSDVEDHNHDLMLLQLRDQASLGS 134

Query: 128  KIQPLPLKNDCSEENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQ 185
            K++P+ L + C++     C + GWG + +   +FPDT+ CA+V + P+++CE AYPG+IT
Sbjct: 135  KVKPISLADHCTQPGQKCTVSGWGTVTSPRENFPDTLNCAEVKIFPQKKCEDAYPGQITD 194

Query: 186  SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
             MVCAG  K G D+CQGDSGGPLVC G L+G+ SWG  PCG  +KPGVYT++C ++ WI+
Sbjct: 195  VMVCAGSSK-GADTCQGDSGGPLVCDGALQGITSWGSDPCGRSDKPGVYTNICRYLDWIK 253

Query: 246  NILRNK 251
             I+ +K
Sbjct: 254  KIIGSK 259


>gi|6679487|ref|NP_032966.1|  protease, serine, 19 [Mus musculus]
gi|33585579|gb|AAH55895.1|  Protease, serine, 19 [Mus musculus]
gi|7229069|dbj|BAA92435.1|  neuropsin [Mus musculus]
gi|2137594|pir||I56559  neuropsin - mouse
gi|6093537|sp|Q61955|NRPN_MOUSE  Neuropsin precursor (NP) (Kallikrein 8)
gi|1020091|dbj|BAA06451.1|  neuropsin [Mus musculus]
gi|1582323|prf||2118319A  neuropsin
          Length = 260

 Score =  239 bits (611), Expect = 4e-62
 Identities = 113/248 (45%), Positives = 159/248 (64%), Gaps = 10/248 (4%)

Query: 13   LCLVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            + L+L    AW+      +  K++ G  C+  S P+QAAL+     L+CGGVL+  +WVLTAA
Sbjct: 13   ILLLLFMGAWAGLTRAQGSKILEGRECIPHSQPWQAALFQGERLICGGVLVGDRWVLTAA 72

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN---PETHDNDIMMVHLKNPVKF 125
            HCKK    V LG H+L+  +  +++I V ++I HP YN   PE H +DIM++ L+N
Sbjct: 73   HCKKQKYSVRLGDHSLQSRDQPEQEIQVAQSIQHPCYNNSNPEDHSHDIMLIRLQNSANL 132

Query: 126  SKKIQPLPLKNDCSEENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKI 183
              K++P+ L N C +    C I GWG + +   +FP+T+ CA+V +   + +CERAYPGKI
Sbjct: 133  GDKVKPVQLANLCPKVGQKCIISGWGTVTSPQENFPNTLNCAEVKIYSQNKCERAYPGKI 192

Query: 184  TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
```

```
           T+ MVCAG    G D+CQGDSGGPLVC G L+G+ SWG  PCG  EKPGVYT +C +  W
Sbjct: 193 TEGMVCAGS-SNGADTCQGDSGGPLVCDGMLQGITSWGSDPCGKPEKPGVYTKICRYTTW 251

Query: 244 IQNILRNK 251
           I+  + N+
Sbjct: 252 IKKTMDNR 259
```

>gi|21464127|ref|NP_653088.1| G kallikrein 8 isoform 2 [Homo sapiens]
gi|5672479|dbj|BAA82666.1| G neuropsin type2 [Homo sapiens]
Length = 305

```
 Score =  238 bits (608), Expect = 8e-62
 Identities = 108/232 (46%), Positives = 158/232 (68%), Gaps = 6/232 (2%)

Query: 25  EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNL 84
           +++KV+ G  C    S P+QAAL+      LLCGGVL+    WVLTAAHCKKP    V LG H+L
Sbjct: 74  QEDKVLGGHECQPHSQPWQAALFQGQQLLCGGVLVGGNWVLTAAHCKKPKYTVRLGDHSL 133

Query: 85  RQTETFQRQISVDRTIVHPRYNP---ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEE 141
           +   +  +++I V ++I HP YN    E H++D+M++ L++      K++P+ L + C++
Sbjct: 134 QNKDGPEQEIPVVQSIPHPCYNSSDVEDHNHDLMLLQLRDQASLGSKVKPISLADHCTQP 193

Query: 142 NPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDS 199
               C + GWG + +   +FPDT+ CA+V + P+++CE AYPG+IT  MVCAG  K G D+
Sbjct: 194 GQKCTVSGWGTVTSPRENFPDTLNCAEVKIFPQKKCEDAYPGQITDGMVCAGSSK-GADT 252

Query: 200 CQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRNK 251
           CQGDSGGPLVC G L+G+ SWG  PCG  +KPGVYT++C ++ WI+ I+ +K
Sbjct: 253 CQGDSGGPLVCDGALQGITSWGSDPCGRSDKPGVYTNICRYLDWIKKIIGSK 304
```

>gi|11545747|ref|NP_071329.1| G kallikrein 14 preproprotein [Homo sapiens]
gi|6715552|gb|AAD50773.2| G kallikrein-like protein 6 [Homo sapiens]
gi|13897995|gb|AAK48524.1| G kallikrein 14 [Homo sapiens]
gi|13897993|gb|AAK48523.1| G kallikrein 14 [Homo sapiens]
gi|10799399|gb|AAG23260.1| G Homo sapiens kallikrein-like protein 6
gi|12230294|sp|Q9P0G3|KLK14_HUMAN G Kallikrein 14 precursor (Kallikrein-like protein
Length = 251

```
 Score =  238 bits (606), Expect = 1e-61
 Identities = 107/241 (44%), Positives = 156/241 (64%), Gaps = 4/241 (1%)

Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGH--LLCGGVLIDPQWVLTAAHCKK 72
           L +A +    E++ K++ G  C + S P+QAAL         LCGG L+  QWV+TAAHC +
Sbjct: 11  LAIAMTQSQEDENKIIGGHTCTRSSQPWQAALLAGPRRRFLCGGALLSGQWVITAAHCGR 70

Query: 73  PNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPL 132
           P LQV LGKHNLR+ E  Q+ + V R + HP YN  THDND+M++ L+ P +  + ++P+
Sbjct: 71  PILQVALGKHNLRRWEATQQVLRVVRQVTHPNYNSRTHDNDLMLLQLQQPARIGRAVRPI 130

Query: 133 PLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCA 190
             +  C+    +C++ GWG + +    +P ++QC ++++ P E C++AYP  IT  MVCA
Sbjct: 131 EVTQACASPGTSCRVSGWGTISSPIARYPASLQCVNINISPDEVCQKAYPRTITPGMVCA 190
```

```
Query: 191 GDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
           G   + G DSCQGDSGGPLVC G+L+GLVSWG    C      PGVYT++C +  WI+  +R+
Sbjct: 191 GVPQGGKDSCQGDSGGPLVCRGQLQGLVSWGMERCALPGYPGVYTNLCKYRSWIEETMRD 250

Query: 251 K 251
           K
Sbjct: 251 K 251
```

>gi|50959826|gb|AAH74905.1| G Kallikrein 14, preproprotein [Homo sapiens]
gi|50959637|gb|AAH74904.1| G Kallikrein 14, preproprotein [Homo sapiens]
Length = 251

Score = 237 bits (605), Expect = 2e-61
Identities = 107/241 (44%), Positives = 156/241 (64%), Gaps = 4/241 (1%)

```
Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGH--LLCGGVLIDPQWVLTAAHCKK 72
           L +A +   E++ K++ G  C + S P+QAAL         LCGG L+  QWV+TAAHC +
Sbjct: 11  LAIAMTRSQEDENKIIGGYTCTRSSQPWQAALLAGPRRRFLCGGALLSGQWVITAAHCGR 70

Query: 73  PNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPL 132
           P LQV LGKHNLR+ E  Q+ + V R + HP YN  THDND+M++ L+ P +  + ++P+
Sbjct: 71  PILQVALGKHNLRRWEATQQVLRVVRQVTHPNYNSRTHDNDLMLLQLQQPARIGRAVRPI 130

Query: 133 PLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCA 190
            +   C+     +C++ GWG + +     +P ++QC ++++ P E C++AYP  IT  MVCA
Sbjct: 131 EVTQACASPGTSCRVSGWGTISSPIARYPASLQCVNINISPDEVCQKAYPRTITPGMVCA 190

Query: 191 GDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
           G   + G DSCQGDSGGPLVC G+L+GLVSWG    C      PGVYT++C +  WI+  +R+
Sbjct: 191 GVPQGGKDSCQGDSGGPLVCRGQLQGLVSWGMERCALPGYPGVYTNLCKYRSWIEETMRD 250

Query: 251 K 251
           K
Sbjct: 251 K 251
```

>gi|34856166|ref|XP_218643.2| G similar to glandular kallikrein KLK13 [Rattus norve
Length = 277

Score = 235 bits (600), Expect = 7e-61
Identities = 110/226 (48%), Positives = 149/226 (65%), Gaps = 7/226 (3%)

```
Query: 32  GGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQ 91
           G  CL   S P+QAAL    G LLCGGVL+ P+WVLTAAHC+K     V LGKH L + E  +
Sbjct: 41  GYTCLPHSQPWQAALLVRGRLLCGGVLVHPKWVLTAAHCRKDGYTVHLGKHALGRVENGE 100

Query: 92  RQISVDRTIVHPRYNPE----THDNDIMMVHLKNPVKFSKKIQPLPLK-NDCSEENPNCQ 146
           + + V R+I HP Y          HD+DIM++ LK+PV+ S  ++ L L  +DC       C+
Sbjct: 101 QAMEVVRSIPHPEYQVSPTHLNHDHDIMLLELKSPVQLSNHVRTLQLSADDCLPTGTCCR 160

Query: 147 ILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDS 204
           + GWG   +   ++P T+QCA++ L   E+C + YPGKIT +M+CAG  + G DSC+GDS
Sbjct: 161 VSGWGTTTSPQVNYPKTLQCANIELRSDEECRQVYPGKITANMLCAGTKEGGKDSCEGDS 220

Query: 205 GGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
           GGPL+C G+L G++SWGD PCG    +PGVYT V   ++RWIQ  +RN
```

```
Sbjct: 221 GGPLICNGKLYGIISWGDFPCGQPNRPGVYTRVSKYLRWIQGTIRN 266
```

>gi|26891548|gb|AAN78420.1| G glandular kallikrein KLK13 [Mus musculus]
Length = 276

```
 Score =  235 bits (600), Expect = 7e-61
 Identities = 117/256 (45%), Positives = 161/256 (62%), Gaps = 19/256 (7%)

Query: 14   CLVLAKSAW-SEEQEKVVHGG-----------PCLKDSHPFQAALYTSGHLLCGGVLIDP 61
            CL LA S    S +   K+++G             CL   S P+QAAL    G LLCGGVL+ P
Sbjct: 10   CLTLALSEGISRDYPKILNGTNGTSGFLPGGYTCLPHSQPWQAALLIRGRLLCGGVLVHP 69

Query: 62   QWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPE----THDNDIMMV 117
            +WVLTAAHC+K      V LGKH  L + E  ++ + V R+I HP Y          HD+DIM++
Sbjct: 70   KWVLTAAHCRKDGYTVHLGKHALGRVENGEQAMEVVRSIPHPEYQVTPTHLNHDHDIMLL 129

Query: 118  HLKNPVKFSKKIQPLPLK-NDCSEENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQ 174
             LK+PV+ S   ++ L L  +DC       C++ GWG    +    ++P T+QCA++ L    E+
Sbjct: 130  ELKSPVQLSSHVRTLKLSADDCLPTGTCCRVSGWGTTTSPQVNYPKTLQCANIELRSDEE 189

Query: 175  CERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVY 234
            C + YPGKIT +M+CAG  + G DSC+GDSGGPL+C G+L G++SWGD PCG  +PGVY
Sbjct: 190  CRQVYPGKITANMLCAGTKEGGKDSCEGDSGGPLICNGKLYGIISWGDFPCGQPNRPGVY 249

Query: 235  TDVCTHIRWIQNILRN 250
            T V   ++RWI+ I+RN
Sbjct: 250  TRVSKYLRWIREIIRN 265
```

>gi|39645087|gb|AAH63763.1| Unknown (protein for MGC:70078) [Mus musculus]
Length = 246

```
 Score =  235 bits (599), Expect = 9e-61
 Identities = 110/226 (48%), Positives = 150/226 (66%), Gaps = 7/226 (3%)

Query: 32   GGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQ 91
            G  CL  S P+QAAL   G LLCGGVL+ P+WVLTAAHC+K     V LGKH L + E  +
Sbjct: 10   GYTCLPHSQPWQAALLIRGRLLCGGVLVHPKWVLTAAHCRKDGYTVHLGKHALGRVENGE 69

Query: 92   RQISVDRTIVHPRYNPE----THDNDIMMVHLKNPVKFSKKIQPLPLK-NDCSEENPNCQ 146
            + + V R+I HP Y          HD+DIM++ LK+PV+ S  ++ L L +DC      C+
Sbjct: 70   QAMEVVRSIPHPEYQVTPTHLNHDHDIMLLELKSPVQLSSHVRTLKLSADDCLPTGTCCR 129

Query: 147  ILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDS 204
            + GWG    +    ++P T+QCA++ L    E+C + YPGKIT +M+CAG  + G DSC+GDS
Sbjct: 130  VSGWGTTTSPQVNYPKTLQCANIELRSDEECRQVYPGKITANMLCAGTKEGGKDSCEGDS 189

Query: 205  GGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            GGPL+C G+L G++SWGD PCG    +PGVYT V  ++RWI+ I+RN
Sbjct: 190  GGPLICNGKLYGIISWGDFPCGQPNRPGVYTRVSKYLRWIREIIRN 235
```

>gi|27731521|ref|XP_218648.1| G similar to Neuropsin precursor (NP) (Kallikrein 8)
protease 1) [Rattus norvegicus]
Length = 260

```
 Score =  234 bits (597), Expect = 2e-60
 Identities = 111/245 (45%), Positives = 155/245 (63%), Gaps = 10/245 (4%)

Query: 13   LCLVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
             + L L    AW+     +  K++ G  C   S P+Q AL+    L+CGGVL+  +WVLTAA
Sbjct: 13   ILLFLLMGAWAGLTRAQGSKILEGQECKPHSQPWQTALFQGERLVCGGVLVGDRWVLTAA 72

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRY---NPETHDNDIMMVHLKNPVKF 125
             HCKK    V LG H+L++ +  +++I V R+I HP +   NPE H +DIM++ L+N
Sbjct: 73   HCKKDKYSVRLGDHSLQKRDEPEQEIQVARSIQHPCFNSSNPEDHSHDIMLIRLQNSANL 132

Query: 126  SKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKI 183
              K++P+ L N C +     C I GWG + +   +FP+T+ CA+V +   + +CERAYPGKI
Sbjct: 133  GDKVKPIELANLCPKVGQKCIISGWGTVTSPQENFPNTLNCAEVKIYSQNKCERAYPGKI 192

Query: 184  TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
             T+ MVCAG     G D+CQGDSGGPLVC G L+G+ SWG  PCG  EKPGVYT +C +   W
Sbjct: 193  TEGMVCAGS-SNGADTCQGDSGGPLVCNGVLQGITSWGSDPCGKPEKPGVYTKICRYTNW 251

Query: 244  IQNIL 248
             I+  +
Sbjct: 252  IKKTM 256
```

>gi|3559978|emb|CAA06643.1| serine protease [Rattus rattus]
gi|6093538|sp|O88780|NRPN_RAT   Neuropsin precursor (NP) (Kallikrein 8) (Brain serine
Length = 260

```
 Score =  233 bits (594), Expect = 4e-60
 Identities = 110/245 (44%), Positives = 155/245 (63%), Gaps = 10/245 (4%)

Query: 13   LCLVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
             + L L    AW+     +  K++ G  C   S P+Q AL+    L+CGGVL+  +WVLTAA
Sbjct: 13   ILLFLLMGAWAGLTRAQGSKILEGQECKPHSQPWQTALFQGERLVCGGVLVGDRWVLTAA 72

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRY---NPETHDNDIMMVHLKNPVKF 125
             HCKK    V LG H+L++ +  +++I V R+I HP +   NPE H +DIM++ L+N
Sbjct: 73   HCKKDKYSVRLGDHSLQKRDEPEQEIQVARSIQHPCFNSSNPEDHSHDIMLIRLQNSANL 132

Query: 126  SKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKI 183
              K++P+ L N C +     C I GWG + +   +FP+T+ CA+V +   + +CERAYPGKI
Sbjct: 133  GDKVKPIELANLCPKVGQKCIISGWGTVTSPQENFPNTLNCAEVKIYSQNKCERAYPGKI 192

Query: 184  TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
             T+ MVCAG     G D+CQGDSGGPLVC G L+G+ +WG  PCG  EKPGVYT +C +   W
Sbjct: 193  TEGMVCAGS-SNGADTCQGDSGGPLVCNGVLQGITTWGSDPCGKPEKPGVYTKICRYTNW 251

Query: 244  IQNIL 248
             I+  +
Sbjct: 252  IKKTM 256
```

>gi|57037485|ref|XP_541468.1| G PREDICTED: similar to kallikrein 8 isoform 1 prepr
familiaris]
Length = 377

Score = 233 bits (593), Expect = 5e-60
Identities = 107/242 (44%), Positives = 158/242 (65%), Gaps = 9/242 (3%)

```
Query: 15   LVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC 70
            L+L   AW+     ++ KV+ G  C   S P+Q AL+    LLCGGVLI+  WVLTAAHC
Sbjct: 133  LLLLLEAWAGHLRAQESKVLGGQECEAHSQPWQTALFQGVRLLCGGVLIEDNWVLTAAHC 192

Query: 71   KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN--PETHDNDIMMVHLKNPVKFSKK 128
            KK    V LG H+L+  ++ +++++V ++I HP YN   E H +D+M++ L+       +
Sbjct: 193  KKRKYTVRLGDHSLKNKDSSEQEMAVAQSIPHPCYNGSNEDHSHDLMLIRLRGRASLGPQ 252

Query: 129  IQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQS 186
            ++P+ L + C E    C I GWG + +   +FPDT+ CA+V + P+++C+  YPG++T
Sbjct: 253  VKPINLADHCPEVGQKCTISGWGTVTSPRENFPDTLNCAEVEIFPQKKCKDVYPGEVTDG 312

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M+CAGD   G DSCQGDSGGPLVCGG L+G+ SWG  PCG  E+PGVYT++C ++ WI+
Sbjct: 313  MICAGD-SNGADSCQGDSGGPLVCGGVLQGITSWGSDPCGRPERPGVYTNICRYLDWIKK 371

Query: 247  IL 248
             +
Sbjct: 372  TI 373
```

>gi|9910298|ref|NP_064358.1| protease, serine, 20 [Mus musculus]
gi|6681653|dbj|BAA88825.1| hippostasin [Mus musculus]
Length = 249

Score = 233 bits (593), Expect = 5e-60
Identities = 106/251 (42%), Positives = 157/251 (62%), Gaps = 9/251 (3%)

```
Query: 6    LTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVL 65
            + ++++AL LV         + +++ G  C   S P+Q AL+    LLCG  LI P+W+L
Sbjct: 1    MILRLIALALVTGHVGG---ETRIIKGYECRPHSQPWQVALFQKTRLLCGATLIAPKWLL 57

Query: 66   TAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----ETHDNDIMMVHLKN 121
            TAAHC+KP+  ++LG+HNL +T+  +++     +  HP +N     + H NDIM+V + +
Sbjct: 58   TAAHCRKPHYVILLGEHNLEKTDGCEQRRMATESFPHPDFNNSLPNKDHRNDIMLVKMSS 117

Query: 122  PVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAY 179
            PV F++ +QPL L   C     +C I GWG   +     P +++CA+V ++  ++CE+AY
Sbjct: 118  PVFFTRAVQPLTLSPHCVAAGTSCLISGWGTTSSPQLRLPHSLRCANVSIIEHKECEKAY 177

Query: 180  PGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCT 239
            PG IT +M+CA   KEG DSCQGDSGGPLVC G L+G++SWG  PC    KPGVYT VC
Sbjct: 178  PGNITDTMLCASVRKEGKDSCQGDSGGPLVCNGSLQGIISWGQDPCAVTRKPGVYTKVCK 237

Query: 240  HIRWIQNILRN 250
            +  WI  ++RN
Sbjct: 238  YFNWIHEVMRN 248
```

>gi|6681654|dbj|BAA36955.1| hippostasin prostate type [Mus musculus]
gi|26365926|dbj|BAB26461.2| unnamed protein product [Mus musculus]
gi|26364453|dbj|BAB26241.2| unnamed protein product [Mus musculus]
Length = 276

```
 Score =  233 bits (593), Expect = 5e-60
 Identities = 106/251 (42%), Positives = 157/251 (62%), Gaps = 9/251 (3%)

Query: 6    LTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVL 65
            + ++++AL LV          + +++ G  C   S P+Q AL+     LLCG  LI P+W+L
Sbjct: 28   MILRLIALALVTGHVGG---ETRIIKGYECRPHSQPWQVALFQKTRLLCGATLIAPKWLL 84

Query: 66   TAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----ETHDNDIMMVHLKN 121
            TAAHC+KP+  ++LG+HNL +T+  +++       +  HP +N      + H NDIM+V + +
Sbjct: 85   TAAHCRKPHYVILLGEHNLEKTDGCEQRRMATESFPHPDFNNSLPNKDHRNDIMLVKMSS 144

Query: 122  PVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAY 179
            PV F++ +QPL L   C      +C I GWG    +       P +++CA+V ++  ++CE+AY
Sbjct: 145  PVFFTRAVQPLTLSPHCVAAGTSCLISGWGTTSSPQLRLPHSLRCANVSIIEHKECEKAY 204

Query: 180  PGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCT 239
            PG IT +M+CA    KEG DSCQGDSGGPLVC G L+G++SWG  PC     KPGVYT VC
Sbjct: 205  PGNITDTMLCASVRKEGKDSCQGDSGGPLVCNGSLQGIISWGQDPCAVTRKPGVYTKVCK 264

Query: 240  HIRWIQNILRN 250
            +   WI  ++RN
Sbjct: 265  YFNWIHEVMRN 275
```

>gi|4699765|pdb|1NPM|B Chain B, Neuropsin, A Serine Protease Expressed In The Lir System Of Mouse Brain
gi|4699764|pdb|1NPM|A Chain A, Neuropsin, A Serine Protease Expressed In The Limbi System Of Mouse Brain
Length = 225

```
 Score =  233 bits (593), Expect = 5e-60
 Identities = 107/225 (47%), Positives = 148/225 (65%), Gaps = 6/225 (2%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            ++ G  C+  S P+QAAL+    L+CGGVL+  +WVLTAAHCKK     V LG H+L+  +
Sbjct: 1    ILEGRECIPHSQPWQAALFQGERLICGGVLVGDRWVLTAAHCKKQKYSVRLGDHSLQSRD 60

Query: 89   TFQRQISVDRTIVHPRY---NPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNC 145
              +++I  V ++I HP Y   NPE H +DIM++ L+N      K++P+ L N C +    C
Sbjct: 61   QPEQEIQVAQSIQHPCYNNSNPEDHSHDIMLIRLQNSANLGDKVKPVQLANLCPKVGQKC 120

Query: 146  QILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGD 203
             I GWG + +    +FP+T+ CA+V +   + +CERAYPGKIT+ MVCAG    G D+CQGD
Sbjct: 121  IISGWGTVTSPQENFPNTLNCAEVKIYSQNKCERAYPGKITEGMVCAGS-SNGADTCQGD 179

Query: 204  SGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            SGGPLVC G L+G+ SWG  PCG  EKPGVYT +C +  WI+ +
Sbjct: 180  SGGPLVCDGMLQGITSWGSDPCGKPEKPGVYTKICRYTTWIKKTM 224
```

>gi|33469049|ref|NP_777355.1| kallikrein 14 [Mus musculus]
gi|26891550|gb|AAN78421.1| glandular kallikrein KLK14 [Mus musculus]
Length = 250

```
 Score =  232 bits (592), Expect = 6e-60
 Identities = 108/252 (42%), Positives = 163/252 (64%), Gaps = 7/252 (2%)
```

```
Query: 3   MKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTS-GH-LLCGGVLID 60
           M +L + + AL + +A+S    +   K++ G  C+++S P+Q AL    GH  LCGGVL+
Sbjct: 1   MFLLLIILQALAVAIAQS---QGDHKIIGGYRCVRNSQPWQVALQAGPGHRFLCGGVLLS 57

Query: 61  PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
            QWV+TAAHC +P L V LGKHN+R+ E  Q+ + V R + HP+Y P+ HDND+M++ L+
Sbjct: 58  DQWVITAAHCARPILHVALGKHNIRRWEATQQVVRVARQVPHPQYQPQAHDNDLMLLKLQ 117

Query: 121 NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERA 178
             V+  + ++ + + + C+      C++ GWG + +    +P  +QC +V+++  + C RA
Sbjct: 118 KKVRLGRAVKTISVASSCASPGTPCRVSGWGTIASPIARYPTALQCVNVNIMSEQACHRA 177

Query: 179 YPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVC 238
           YPG IT  MVCAG  + G DSCQGDSGGPLVCGG+L+GLVSWG   C      PGVY ++C
Sbjct: 178 YPGIITSGMVCAGVPEGGKDSCQGDSGGPLVCGGQLQGLVSWGMERCAMPGYPGVYANLC 237

Query: 239 THIRWIQNILRN 250
            +  WIQ  +++
Sbjct: 238 NYHSWIQRTMQS 249
```

>gi|34856164|ref|XP_218641.2| G similar to glandular kallikrein KLK14 [Rattus norve

Length = 297

Score = 231 bits (589), Expect = 1e-59
Identities = 104/232 (44%), Positives = 151/232 (65%), Gaps = 4/232 (1%)

```
Query: 23  SEEQEKVVHGGPCLKDSHPFQAALYTSG--HLLCGGVLIDPQWVLTAAHCKKPNLQVILG 80
           S+  +K++ G  C+++S P+Q AL        LCGGVL+  QWV+TAAHC +P L V LG
Sbjct: 65  SQGDDKILGGYTCVQNSQPWQVALQAGPGRRFLCGGVLLSDQWVITAAHCARPLLHVALG 124

Query: 81  KHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSE 140
           KHNLR+ E  Q+ + V R + HP+Y P+ HDND+M++ L+  V+  + ++ +P+    C+
Sbjct: 125 KHNLRRWEATQQVLRVVRQVPHPQYRPQAHDNDLMLLKLQRKVRLGRAVRTIPVARSCAS 184

Query: 141 ENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGND 198
              C++ GWG  +     +P  +QC +V+++P + C RAYPG IT  MVCAG  + G D
Sbjct: 185 PGTPCRVSGWGTTASPIVRYPTALQCVNVNIMPEQVCHRAYPGTITSGMVCAGVPEGGKD 244

Query: 199 SCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
           SCQGDSGGPLVC G+L+GLVSWG   C     PGVYT++C +  WIQ  +++
Sbjct: 245 SCQGDSGGPLVCQGQLQGLVSWGMERCAMPGYPGVYTNLCNYHSWIQRTMQS 296
```

>gi|28422450|gb|AAH44756.1| G Klk14 protein [Mus musculus]

Length = 242

Score = 230 bits (587), Expect = 2e-59
Identities = 104/234 (44%), Positives = 153/234 (65%), Gaps = 4/234 (1%)

```
Query: 21  AWSEEQEKVVHGGPCLKDSHPFQAALYTS-GH-LLCGGVLIDPQWVLTAAHCKKPNLQVI 78
           A S+    K++ G  C+++S P+Q AL    GH  LCGGVL+  QWV+TAAHC +P L V
Sbjct: 8   AQSQGDHKIIGGYRCVRNSQPWQVALQAGPGHRFLCGGVLLSDQWVITAAHCARPILHVA 67

Query: 79  LGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDC 138
           LGKHN+R+ E  Q+ + V R + HP+Y P+ HDND+M++ L+  V+  + ++ + + + C
```

```
Sbjct: 68  LGKHNIRRWEATQQVVRVARQVPHPQYQPQAHDNDLMLLKLQKKVRLGRAVKTISVASSC 127

Query: 139 SEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEG 196
           +      C++ GWG + +     +P   +QC +V+++    + C RAYPG IT   MVCAG   + G
Sbjct: 128 ASPGTPCRVSGWGTIASPIARYPTALQCVNVNIMSEQACHRAYPGIITSGMVCAGVPEGG 187

Query: 197 NDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            DSCQGDSGGPLVCGG+L+GLVSWG    C      PGVY ++C +  WIQ  +++
Sbjct: 188 KDSCQGDSGGPLVCGGQLQGLVSWGMERCAMPGYPGVYANLCNYHSWIQRTMQS 241
```

>gi|34856172|ref|XP_218607.2| similar to prostin [Rattus norvegicus]
Length = 480

Score = 229 bits (585), Expect = 4e-59
Identities = 110/261 (42%), Positives = 159/261 (60%), Gaps = 13/261 (4%)

```
Query: 2   PMKMLTMKML-ALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID 60
           P K L+ KML  + L L   S  S++ +KV+ G  C+   S P+Q AL+  G    CG  LI
Sbjct: 218 PDKSLSAKMLQCVDLTLMSSDVSQDGDKVLEGEECVPHSQPWQVALFERGRFNCGAFLIS 277

Query: 61  PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
           P WVLTAAHC+    ++V LG+HNLR+ +   ++  SV R I HP Y   TH +DIM++ L
Sbjct: 278 PHWVLTAAHCQTRFMRVRLGEHNLRKFDGPEQLRSVSRIIPHPGYEARTHRHDIMLLRLF 337

Query: 121 NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGD------------FPDTIQCADVH 168
            P + + +++P+ L   C      +C + GWG + +             PDT+ CA++
Sbjct: 338 RPARLTPQVRPVALPTRCPLLGEDCVVSGWGLLSDNSPGATGSHKSQVRLPDTLHCANIS 397

Query: 169 LVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSK 228
           ++     C + YPG++  +MVCAG    G DSC+GDSGGPLVCGG L+G+VSWGD+PC +
Sbjct: 398 IISEASCNKDYPGRVLPTMVCAGVEGGGTDSCEGDSGGPLVCGGALQGIVSWGDVPCDTT 457

Query: 229 EKPGVYTDVCTHIRWIQNILR 249
            KPGVYT VC+++  WI+  +R
Sbjct: 458 TKPGVYTKVCSYMDWIRKNMR 478
```

>gi|34856168|ref|XP_218645.2| similar to hippostasin prostate type [Rattus norvec

Length = 270

Score = 228 bits (582), Expect = 9e-59
Identities = 105/252 (41%), Positives = 156/252 (61%), Gaps = 9/252 (3%)

```
Query: 5   MLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
           M+ ++ +AL LV           + +++ G  C   S P+Q AL+    LLCG  LI P+W+
Sbjct: 21  MMILRFIALALVTGHVGG---ETRIIKGYECRPHSQPWQVALFQKTRLLCGATLIAPKWL 77

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----ETHDNDIMMVHLK 120
           LTAAHC+KP+   ++LG+HNL +T+ · +++       +  HP +N      + H NDIM+V +
Sbjct: 78  LTAAHCRKPHYVILLGEHNLEKTDGCEQRRMATESFPHPGFNNSLPNKDHRNDIMLVKMS 137

Query: 121 NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERA 178
           +P    ++ ++PL L + C      +C I GWG   +     P +++CA+V ++  ++CERA
Sbjct: 138 SPAFITRAVRPLTLSSLCVTAGTSCLISGWGTTSSPQLRLPHSLRCANVSIIGHKECERA 197

Query: 179 YPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVC 238
```

```
             YPG IT +M+CA   KEG DSCQGDSGGPLVC G L+G++SWG  PC    KPGVYT VC
Sbjct: 198  YPGNITDTMLCASVRKEGKDSCQGDSGGPLVCNGSLQGIISWGQDPCAVTRKPGVYTKVC 257

Query: 239  THIRWIQNILRN 250
              +  WI  ++RN
Sbjct: 258  KYFDWIHEVMRN 269
```

>gi|11244759|gb|AAG33354.1| G ACO protease [Homo sapiens]
Length = 247

```
 Score =  228 bits (580), Expect = 1e-58
 Identities = 102/243 (41%), Positives = 154/243 (63%), Gaps = 4/243 (1%)

Query: 10   MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
             +L L   +LA +A +++ +K++ G  C   S P+Q ALY   G    CG   LI P WVL+AAH
Sbjct: 4    LLTLSFLLASTA-AQDGDKLLEGDECAPHSQPWQVALYERGRFNCGASLISPHWVLSAAH 62

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
             C+     ++V LG+HNLR+ +   ++   +   R I HPRY    +H NDIM++ L   P + + ++
Sbjct: 63   CQSRFMRVRLGEHNLRKRDGPEQLRTTSRVIPHPRYEARSHRNDIMLLRLVQPARLNPQV 122

Query: 130  QPLPLKNDCSEENPNCQILGWGKMENGD---FPDTIQCADVHLVPREQCERAYPGKITQS 186
             +P  L   C       C + GWG +          PDT+ CA++ ++     C+++YPG++T +
Sbjct: 123  RPAVLPTRCPHPGEACVVSGWGLVPLSSPVSLPDTLHCANISIISDTSCDKSYPGRLTNT 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
             MVCAG     G +SC+GDSGGPLVCGG L+G+VSWGD+PC +   KPGVYT VC ++ WI+
Sbjct: 183  MVCAGAEGRGAESCEGDSGGPLVCGGILQGIVSWGDVPCDNTTKPGVYTKVCHYLEWIRE 242

Query: 247  ILR 249
              ++
Sbjct: 243  TMK 245
```

>gi|47480780|gb|AAH69507.1| G Kallikrein 15, isoform 4 preproprotein [Homo sapiens]
gi|20302143|ref|NP_059979.2| G kallikrein 15 isoform 4 preproprotein [Homo sapiens]
gi|9957760|gb|AAG09469.1| G KLK15 [Homo sapiens]
gi|18202940|sp|Q9H2R5|KLK15_HUMAN G Kallikrein 15 precursor (ACO protease)
Length = 256

```
 Score =  227 bits (578), Expect = 3e-58
 Identities = 102/252 (40%), Positives = 156/252 (61%), Gaps = 13/252 (5%)

Query: 10   MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
             +L L   +LA +A +++ +K++ G  C   S P+Q ALY   G    CG   LI P WVL+AAH
Sbjct: 4    LLTLSFLLASTA-AQDGDKLLEGDECAPHSQPWQVALYERGRFNCGASLISPHWVLSAAH 62

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
             C+     ++V LG+HNLR+ +   ++   +   R I HPRY    +H NDIM++ L   P + + ++
Sbjct: 63   CQSRFMRVRLGEHNLRKRDGPEQLRTTSRVIPHPRYEARSHRNDIMLLRLVQPARLNPQV 122

Query: 130  QPLPLKNDCSEENPNCQILGWGKMENGD------------FPDTIQCADVHLVPREQCER 177
             +P  L   C       C + GWG + + +              PDT+ CA++ ++     C++
Sbjct: 123  RPAVLPTRCPHPGEACVVSGWGLVSHNEPGTAGSPRSQVSLPDTLHCANISIISDTSCDK 182
```

```
Query: 178 AYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDV 237
           +YPG++T +MVCAG     G +SC+GDSGGPLVCGG L+G+VSWGD+PC +   KPGVYT V
Sbjct: 183 SYPGRLTNTMVCAGAEGRGAESCEGDSGGPLVCGGILQGIVSWGDVPCDNTTKPGVYTKV 242

Query: 238 CTHIRWIQNILR 249
           C ++ WI+  ++
Sbjct: 243 CHYLEWIRETMK 254
```

>gi|47480768|gb|AAH69480.1| G Kallikrein 15, isoform 4 preproprotein [Homo sapiens]
gi|47479543|gb|AAH69518.1| G Kallikrein 15, isoform 4 preproprotein [Homo sapiens]
Length = 255

Score = 226 bits (576), Expect = 4e-58
Identities = 102/252 (40%), Positives = 155/252 (61%), Gaps = 14/252 (5%)

```
Query: 10  MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
           +L L  +LA +A  ++ +K++ G  C   S P+Q ALY  G   CG  LI P WVL+AAH
Sbjct: 4   LLTLSFLLASTA--QDGDKLLEGDECAPHSQPWQVALYERGRFNCGASLISPHWVLSAAH 61

Query: 70  CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
           C+    ++V LG+HNLR+ +  ++   +  R I HPRY   +H NDIM++ L   P + + ++
Sbjct: 62  CQSRFMRVRLGEHNLRKRDGPEQLRTTSRVIPHPRYEARSHRNDIMLLRLVQPARLNPQV 121

Query: 130 QPLPLKNDCSEENPNCQILGWGKMENGD------------FPDTIQCADVHLVPREQCER 177
           +P  L   C     C + GWG + + +                 PDT+ CA++ ++    C++
Sbjct: 122 RPAVLPTRCPHPGEACVVSGWGLVSHNEPGTAGSPRSQVSLPDTLHCANISIISDTSCDK 181

Query: 178 AYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDV 237
           +YPG++T +MVCAG     G +SC+GDSGGPLVCGG L+G+VSWGD+PC +   KPGVYT V
Sbjct: 182 SYPGRLTNTMVCAGAEGRGAESCEGDSGGPLVCGGILQGIVSWGDVPCDNTTKPGVYTKV 241

Query: 238 CTHIRWIQNILR 249
           C ++ WI+  ++
Sbjct: 242 CHYLEWIRETMK 253
```

>gi|14484922|gb|AAK62813.1| G prostinogen [Homo sapiens]
Length = 255

Score = 226 bits (575), Expect = 6e-58
Identities = 102/252 (40%), Positives = 155/252 (61%), Gaps = 14/252 (5%)

```
Query: 10  MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
           +L L  +LA +A  ++ +K++ G  C   S P+Q ALY  G   CG  LI P WVL+AAH
Sbjct: 4   LLTLSFLLASTA--QDGDKLLEGDECAPHSQPWQVALYERGRFNCGASLISPHWVLSAAH 61

Query: 70  CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
           C+    ++V LG+HNLR+ +  ++   +  R I HPRY   +H NDIM++ L   P + + ++
Sbjct: 62  CQSRFMRVRLGEHNLRKRDGPEQLRTTSRVIPHPRYEARSHRNDIMLLRLVQPARLNPQV 121

Query: 130 QPLPLKNDCSEENPNCQILGWGKMENGD------------FPDTIQCADVHLVPREQCER 177
           +P  L   C     C + GWG + + +                 PDT+ CA++ ++    C++
Sbjct: 122 RPAVLPTRCPHPGEACVVSGWGLVSHNEPGTAGSPRSQVSLPDTLHCANIGIISDTSCDK 181

Query: 178 AYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDV 237
           +YPG++T +MVCAG     G +SC+GDSGGPLVCGG L+G+VSWGD+PC +   KPGVYT V
```

```
Sbjct: 182  SYPGRLTNTMVCAGAEGRGAESCEGDSGGPLVCGGILQGIVSWGDVPCDNTTKPGVYTKV 241

Query: 238  CTHIRWIQNILR 249
            C ++ WI+  ++
Sbjct: 242  CHYLEWIRETMK 253
```

>gi|12834991|dbj|BAB23113.1| unnamed protein product [Mus musculus]
Length = 293

Score = 225 bits (573), Expect = 1e-57
Identities = 97/232 (41%), Positives = 154/232 (66%), Gaps = 5/232 (2%)

```
Query: 23   SEEQEKVVHGGPCLKDSHPFQAALYTSGH-LLCGGVLIDPQWVLTAAHCKKPNLQVILGK 81
            S+   ++V+G  C KD+ P+Q AL    + L CG VLI PQW+LTAAHC+KP  ++ LG
Sbjct: 62   SDSSSRIVNGSDCQKDAQPWQGALLLGPNKLYCGAVLISPQWLLTAAHCRKPVFRIRLGH 121

Query: 82   HNLRQT-ETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSE 140
            H++    E+ Q+     ++I HP Y+   H ND+M++ +   ++ S  ++P+ +  DC+
Sbjct: 122  HSMSPVYESGQQMFQGIKSIPHPGYSHPGHSNDLMLIKMNRKIRDSHSVKPVEIACDCAT 181

Query: 141  ENPNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGND 198
            E   C + GWG     + +FP  +QC ++ ++  E+C+ +YPG+I ++M CAGD +EG D
Sbjct: 182  EGTRCMVSGWGTTSSSHNNFPKVLQCLNITVLSEERCKNSYPGQIDKTMFCAGD-EEGRD 240

Query: 199  SCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            SCQGDSGGP+VC G+L+GLVSWGD PC  + +PGVYT++C  ++WI++ + +
Sbjct: 241  SCQGDSGGPVVCNGKLQGLVSWGDFPCAQRNRPGVYTNLCEFVKWIKDTMNS 292
```

>gi|57037473|ref|XP_541465.1| PREDICTED: similar to glandular kallikrein KLK13 [(
Length = 328

Score = 224 bits (572), Expect = 1e-57
Identities = 106/226 (46%), Positives = 145/226 (64%), Gaps = 7/226 (3%)

```
Query: 32   GGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQ 91
            G  C   S P+QAAL   G L CGGVL+ P+WVLTAAHC K   +V LGKH L + E  +
Sbjct: 90   GYTCRPHSQPWQAALLVQGRLFCGGVLVHPKWVLTAAHCLKDGYRVYLGKHALGRVEAGE 149

Query: 92   RQISVDRTIVHPRYNPE----THDNDIMMVHLKNPVKFSKKIQPLPLK-NDCSEENPNCQ 146
            +   V R+I HP+Y        HD+DIM++ L++PV+ +  I+ LPL  N+C      C+
Sbjct: 150  QVREVVRSIPHPQYQISPTHLNHDHDIMLLELQSPVQPTNHIRVLPLSHNNCLPAGTCCR 209

Query: 147  ILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDS 204
            + GWG   +    +P T+QCA++ L   E+C + YPGKIT +M+CAG  + G DSC+GDS
Sbjct: 210  VSGWGTTTSPQVSYPQTLQCANIQLRSDEECRQVYPGKITPNMLCAGTKEGGKDSCEGDS 269

Query: 205  GGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            GGPL+C G L G++SWGD PCG   +PGVYT V  ++ WI+  +RN
Sbjct: 270  GGPLICNGTLHGIISWGDFPCGQPNRPGVYTRVSQYVLWIRETIRN 315
```

>gi|33585653|gb|AAH56068.1| LOC397853 protein [Xenopus laevis]
Length = 248

```
 Score =  224 bits (572), Expect = 1e-57
 Identities = 106/244 (43%), Positives = 155/244 (63%), Gaps = 4/244 (1%)

Query: 7   TMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLT 66
            TMK L + ++L  +    E+ +K+V G   C K++ P+Q +L   +G+   CGG LI+ QWV++
Sbjct: 4   TMKFLVILVLLGAAVAFEDDDKIVGGFTCAKNAVPYQVSL-NAGYHFCGGSLINSQWVVS 62

Query: 67  AAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFS 126
            AAHC K   +QV LG+HN+    E  ++ I   + I HP YN    DNDIM++ L    + S
Sbjct: 63  AAHCYKSRIQVRLGEHNIALNEGTEQFIDSQKVIKHPNYNSRNLDNDIMLIKLSTTARLS 122

Query: 127 KKIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKIT 184
              IQ +PL + C+     NC I GWG  + +G ++PD +QC +   ++   QC  +YPG+IT
Sbjct: 123 ANIQSVPLPSACASAGTNCLISGWGNTLSSGTNYPDLLQCLNAPILTDSQCSNSYPGEIT 182

Query: 185 QSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWI 244
            ++M CAG +   G DSCQGDSGGP+VC G+L+G+VSWG    C  +  PGVYT VC   + WI
Sbjct: 183 KNMFCAGFLAGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRNYPGVYTKVCNFVTWI 241

Query: 245 QNIL 248
            Q+ +
Sbjct: 242 QSTI 245
```

>gi|33469045|ref|NP_777354.1| G kallikrein 15 [Mus musculus]
gi|26891552|gb|AAN78422.1| G prostin [Mus musculus]

```
          Length = 254

 Score =  224 bits (571), Expect = 2e-57
 Identities = 107/252 (42%), Positives = 156/252 (61%), Gaps = 14/252 (5%)

Query: 11  LALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC 70
            L L  VL  SA +++ +KV+ G  C+  S P+Q AL+   G   CG  LI P+WVLTAAHC
Sbjct: 3   LLLAFVLLVSA-AQDGDKVLEGEECVPHSQPWQVALFERGRFNCGAFLISPRWVLTAAHC 61

Query: 71  KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQ 130
            +   ++V LG+HNLR+ +  ++  SV R I HP Y   TH +DIM++ L  P + +  ++
Sbjct: 62  QTRFMRVRLGEHNLRKFDGPEQLRSVSRIIPHPGYEARTHRHDIMLLRLFKPARLTAYVR 121

Query: 131 PLPLKNDCSEENPNCQILGWGKMENGD------------FPDTIQCADVHLVPREQCERA 178
            P+ L   C     +C + GWG + + +            PDT+ CA++ ++    C +
Sbjct: 122 PVALPRRCPLIGEDCVVSGWGLLSDNNPGATGSQKSHVRLPDTLHCANISIISEASCNKD 181

Query: 179 YPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVC 238
            YPG++  +MVCAG   G DSC+GDSGGPLVCGG L+G+VSWGD+PC +  KPGVYT VC
Sbjct: 182 YPGRVLPTMVCAGVEGGGTDSCEGDSGGPLVCGGALQGIVSWGDVPCDTTTKPGVYTKVC 241

Query: 239 THIRWI-QNILR 249
            +++ WI +N+ R
Sbjct: 242 SYLEWIWENVRR 253
```

>gi|47481100|gb|AAH69334.1| G Kallikrein 13, precursor [Homo sapiens]
gi|47480821|gb|AAH69543.1| G Kallikrein 13, precursor [Homo sapiens]
gi|11496281|ref|NP_056411.1| G kallikrein 13 precursor [Homo sapiens]
gi|6063386|gb|AAD26425.2| G kallikrein-like protein 4 KLK-L4 [Homo sapiens]

gi|10799398|gb|AAG23259.1| G kallikrein 13 [Homo sapiens]
gi|9296990|sp|Q9UKR3|KLK13_HUMAN G Kallikrein 13 precursor (Kallikrein-like protein
Length = 277

```
 Score =  224 bits (571), Expect = 2e-57
 Identities = 118/271 (43%), Positives = 162/271 (59%), Gaps = 24/271 (8%)

Query: 6    LTMKMLALCLVLAKSAWSEEQEKVVH----------GGPCLKDSHPFQAALYTSGHLLCG 55
            L + + +L L L+    S+E  KV++          G  C   S P+QAAL    G LLCG
Sbjct: 4    LALVIASLTLALSGGV-SQESSKVLNTNGTSGFLPGGYTCFPHSQPWQAALLVQGRLLCG 62

Query: 56   GVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPE----THD 111
            GVL+ P+WVLTAAHC K  L+V LGKH L + E  ++    V  +I HP Y       HD
Sbjct: 63   GVLVHPKWVLTAAHCLKEGLKVYLGKHALGRVEAGEQVREVVHSIPHPEYRRSPTHLNHD 122

Query: 112  NDIMMVHLKNPVKFSKKIQPLPLK-NDCSEENPNCQILGWGKMENG--DFPDTIQCADVH 168
            +DIM++ L++PV+ +  IQ LPL  N+        C++ GWG    +    ++P T+QCA++
Sbjct: 123  HDIMLLELQSPVQLTGYIQTLPLSHNNRLTPGTTCRVSGWGTTTSPQVNYPKTLQCANIQ 182

Query: 169  LVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSK 228
            L   E+C + YPGKIT +M+CAG  + G DSC+GDSGGPLVC    L G+VSWGD PCG
Sbjct: 183  LRSDEECRQVYPGKITDNMLCAGTKEGGKDSCEGDSGGPLVCNRTLYGIVSWGDFPCGQP 242

Query: 229  EKPGVYTDVCTHIRWIQNILR------NKWL 253
            ++PGVYT V  ++ WI+  +R      KWL
Sbjct: 243  DRPGVYTRVSRYVLWIRETIRKYETQQQKWL 273
```

>gi|49256006|gb|AAH73410.1| G LOC397853 protein [Xenopus laevis]
Length = 255

```
 Score =  224 bits (571), Expect = 2e-57
 Identities = 106/244 (43%), Positives = 155/244 (63%), Gaps = 4/244 (1%)

Query: 7    TMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLT 66
            TMK L + ++L  +   E+ +K+V G  C K++ P+Q +L  +G+  CGG LI+ QWV++
Sbjct: 11   TMKFLVILVLLGAAVAFEDDDKIVGGFTCAKNAVPYQVSL-NAGYHFCGGSLINSQWVVS 69

Query: 67   AAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFS 126
            AAHC K  +QV LG+HN+   E   ++ I   + I HP YN   DNDIM++ L    + S
Sbjct: 70   AAHCYKSRIQVRLGEHNIALNEGTEQFIDSQKVIKHPNYNSRNLDNDIMLIKLSTTARLS 129

Query: 127  KKIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKIT 184
              IQ +PL + C+    NC I GWG  + +G ++PD +QC +  ++   QC  +YPG+IT
Sbjct: 130  ANIQSVPLPSACASAGTNCLISGWGNTLSSGTNYPDLLQCLNAPVLTDSQCSNSYPGEIT 189

Query: 185  QSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWI 244
            ++M CAG +  G DSCQGDSGGP+VC G+L+G+VSWG   C  + + PGVYT VC  + WI
Sbjct: 190  KNMFCAGFLAGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRNYPGVYTKVCNFVTWI 248

Query: 245  QNIL 248
            Q+ +
Sbjct: 249  QSTI 252
```

>gi|59808136|gb|AAH89741.1| Unknown (protein for MGC:108396) [Xenopus tropicalis]
Length = 244

```
Score =  224 bits (570), Expect = 2e-57
Identities = 105/243 (43%), Positives = 154/243 (63%), Gaps = 4/243 (1%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK L + ++L  +   E+ +K+V G  C K++ P+Q +L  +G+  CGG LI+ QWV++A
Sbjct: 1    MKFLIVLVLLGAAVAFEDDDKIVGGFTCTKNAVPYQVSL-NAGYHFCGGSLINSQWVVSA 59

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K  +QV LG+HN+   E  ++ I   + I HP YN    DNDIM++ L     + S
Sbjct: 60   AHCYKSRIQVRLGEHNIAVNEGTEQFIESQKVIKHPSYNSRNLDNDIMLIKLSTTARLSS 119

Query: 128  KIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQ 185
             IQ +PL + C+    NC I GWG  + +G ++PD +QC +  ++   +C  +YPG+IT
Sbjct: 120  NIQSVPLPSACASAGTNCLISGWGNTLSSGTNYPDLLQCLNAPILTASECSNSYPGEITN 179

Query: 186  SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            +M CAG +  G DSCQGDSGGP+VC G+L+G+VSWG   C   +  PGVYT VC ++ WIQ
Sbjct: 180  NMFCAGFLAGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRNYPGVYTKVCNYVSWIQ 238

Query: 246  NIL 248
            N +
Sbjct: 239  NTI 241
```

>gi|65163|emb|CAA37538.1| G unnamed protein product [Xenopus laevis]
gi|104227|pir||A35871 trypsin (EC 3.4.21.4) precursor, pancreatic - African clawed f
gi|136433|sp|P19799|TRY1 XENLA Trypsin precursor
Length = 243

```
Score =  223 bits (569), Expect = 3e-57
Identities = 109/243 (44%), Positives = 156/243 (64%), Gaps = 5/243 (2%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK L LC++L  +A + + +K++ G  C K S P+  +L  SG+  CGG LI  QWV++A
Sbjct: 1    MKFLLLCVLLGAAA-AFDDDKIIGGATCAKSSVPYIVSL-NSGYHFCGGSLITNQWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K ++QV LG+HN+  +E  ++ IS  + I H  YN  T DNDIM++ L +P  +
Sbjct: 59   AHCYKASIQVRLGEHNIALSEGTEQFISSSKVIRHSGYNSYTLDNDIMLIKLSSPASLNA 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQ 185
             +  +PL + CS    +C I GWG  + NG ++PD +QC +  ++   QC  AYPG+IT
Sbjct: 119  AVNTVPLPSGCSAAGTSCLISGWGNTLSNGSNYPDLLQCLNAPILTNAQCNSAYPGEITA 178

Query: 186  SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            +M+C G M+ G DSCQGDSGGP+VC G+L+G+VSWG   C  +  PGVYT VC +  WIQ
Sbjct: 179  NMICVGYMEGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAMRNYPGVYTKVCNYNAWIQ 237

Query: 246  NIL 248
            N +
Sbjct: 238  NTI 240
```

>gi|32484229|gb|AAH54194.1| G MGC64344 protein [Xenopus laevis]
Length = 243

```
 Score =  223 bits (569), Expect = 3e-57
 Identities = 109/243 (44%), Positives = 156/243 (64%), Gaps = 5/243 (2%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK L LC++L  +A + + +K++ G  C K S P+  +L  SG+  CGG LI  QWV++A
Sbjct: 1    MKFLLLCVLLGAAA-AFDDDKIIGGATCAKSSVPYIVSL-NSGYHFCGGSLITNQWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K ++QV LG+HN+  +E  ++ IS  + I H  YN  T DNDIM++ L +P   +
Sbjct: 59   AHCYKASIQVRLGEHNIALSEGTEQFISSSKVIRHSGYNSYTLDNDIMLIKLSSPASLNA 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQ 185
             +  +PL + CS    +C I GWG  + NG ++PD +QC +  ++    QC  AYPG+IT
Sbjct: 119  AVNTVPLPSGCSAAGTSCLISGWGNTLSNGSNYPDLLQCLNAPILTNAQCNSAYPGEITA 178

Query: 186  SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            +M+C G M+ G DSCQGDSGGP+VC G+L+G+VSWG   C  +  PGVYT VC +  WIQ
Sbjct: 179  NMICVGFMEGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAMRNYPGVYTKVCNYNAWIQ 237

Query: 246  NIL 248
            N +
Sbjct: 238  NTI 240
```

>gi|57037469|ref|XP_541464.1| G PREDICTED: similar to kallikrein 14 preproprotein familiaris]
Length = 492

```
 Score =  223 bits (569), Expect = 3e-57
 Identities = 98/231 (42%), Positives = 153/231 (66%), Gaps = 4/231 (1%)

Query: 25   EQEKVVHGGPCLKDSHPFQAALYTSG--HLLCGGVLIDPQWVLTAAHCKKPNLQVILGKH 82
            ++ K++ G  C+++S P+QAAL        LCGG L+  QWV+TAAHC +P L++ LGKH
Sbjct: 262  DENKIIGGYTCIQNSQPWQAALLAGPFRRFLCGGALLSRQWVITAAHCARPILRIALGKH 321

Query: 83   NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
            NL+  E  Q+ + V R + HP+YN +TH+ND+M++ L+ P++  + ++P+ + + C+
Sbjct: 322  NLKNWEATQQVLRVVRQVPHPQYNSQTHNNDLMLLQLERPIQLGRAVRPITIASSCARPG 381

Query: 143  PNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
             +C + GWG   +    +P+++QC ++++   ++C +AY   IT  MVCAG  + G DSC
Sbjct: 382  TSCLVSGWGTTSSPIVRYPNSLQCVNINISSDQECRQAYSQAITVGMVCAGVPQGGKDSC 441

Query: 201  QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRNK 251
            QGDSGGPLVC G+L+GLVSWG   C     PGVYT++C +  WIQN + +K
Sbjct: 442  QGDSGGPLVCKGQLQGLVSWGMEHCALPGYPGVYTNLCKYRTWIQNTIWSK 492
```

>gi|51714013|ref|XP_489832.1| G similar to trypsinogen 10 [Mus musculus]
gi|2358087|gb|AAB69058.1| trypsinogen 10 [Mus musculus]
Length = 246

```
 Score =  223 bits (568), Expect = 4e-57
 Identities = 108/242 (44%), Positives = 159/242 (65%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
```

```
Sbjct: 4   LLFLALVGAAVAFPVDDDDKIVGGYTCRENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
           HC K  +QV LG+HN+    E  ++ I      I HP++  +T DNDIM++ L +PV  + +
Sbjct: 63  HCYKSRIQVRLGEHNINVLEGNEQFIDAANIIKHPKFKKKTLDNDIMLIKLSSPVTLNAR 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
           +   + L + C+      C I GWG  + +G + PD +QC D   L+P+   CE +YPGKIT++
Sbjct: 123 VATVALPSSCAAAGTQCLISGWGNTLSSGVNNPDLLQCLDAPLLPQADCEASYPGKITKN 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
           M+C G ++ G DSCQGDSGGP+VC G+L+G+VSWG   C  K+ PGVYT VC ++ WIQN
Sbjct: 183 MICVGFLEGGKDSCQGDSGGPVVCNGQLQGIVSWG-YGCAQKDNPGVYTKVCNYVDWIQN 241

Query: 247 IL 248
            +
Sbjct: 242 TI 243
```

>gi|2499865|sp|P70059|TRY2_XENLA Trypsin precursor
gi|1621633|gb|AAB17274.1| G trypsinogen [Xenopus laevis]
Length = 244

Score = 223 bits (567), Expect = 5e-57
Identities = 105/243 (43%), Positives = 154/243 (63%), Gaps = 4/243 (1%)

```
Query: 8   MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
           MK L + ++L  +   E+ +K+V G  C K++ P+Q +L  +G+  CGG LI+ QWV++A
Sbjct: 1   MKFLVILVLLGAAVAFEDDDKIVGGFTCAKNAVPYQVSL-NAGYHFCGGSLINSQWVVSA 59

Query: 68  AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
           AHC K  +QV LG+HN+   E  ++ I   + I HP YN    DNDIM++ L    + S
Sbjct: 60  AHCYKSRIQVRLGEHNIALNEGTEQFIDSQKVIKHPNYNSRNLDNDIMLIKLSTTARLSA 119

Query: 128 KIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQ 185
            IQ +PL + C+    NC I GWG  + +G ++PD +QC +  ++   QC  +YPG+IT+
Sbjct: 120 NIQSVPLPSACASAGTNCLISGWGNTLSSGTNYPDLLQCLNAPILTDSQCSNSYPGEITK 179

Query: 186 SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
           +M CAG +  G DSCQGDSGGP+VC G+L+G+VSWG   C  +  PGVYT VC  + WIQ
Sbjct: 180 NMFCAGFLAGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRNYPGVYTKVCNFVTWIQ 238

Query: 246 NIL 248
           + +
Sbjct: 239 STI 241
```

>gi|42759849|gb|AAS45302.1| KLK15 [Saguinus oedipus]
Length = 255

Score = 221 bits (564), Expect = 1e-56
Identities = 100/252 (39%), Positives = 154/252 (61%), Gaps = 14/252 (5%)

```
Query: 10  MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
           +L L  +L  +A  ++  K++ G  C   S P+Q ALY  G   CG  LI P WVL+AAH
Sbjct: 4   LLPLSFLLTSTA--QDGGKLLEGEECAPHSQPWQVALYERGRFNCGASLISPHWVLSAAH 61
```

```
Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C+   ++V LG+HNLR+ +   ++   +   R I HPRY    +H +DIM++ L   P + + ++
Sbjct: 62   CQSRFMRVRLGEHNLRKRDGPEQLRTASRVIPHPRYEARSHRHDIMLLRLVQPARLTPQV 121

Query: 130  QPLPLKNDCSEENPNCQILGWGKMENGD------------FPDTIQCADVHLVPREQCER 177
            +P+ L     C        C + GWG + + +            PDT+ CA++ ++    C++
Sbjct: 122  RPVVLPTRCPHPGEACVVSGWGLVSHNEPGTTGRPQSQVSLPDTLHCANISIISDASCDK 181

Query: 178  AYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDV 237
             YPG++T +MVCAG     G +SC+GDSGGPLVCGG L+G+VSWGD+PC +   KPGVYT V
Sbjct: 182  NYPGRLTNTMVCAGAEGRGAESCEGDSGGPLVCGGILQGIVSWGDVPCDNTTKPGVYTKV 241

Query: 238  CTHIRWIQNILR 249
            C +++WI+  ++
Sbjct: 242  CRYVKWIRETMK 253
```

>gi|37183146|gb|AAQ89373.1| KLK11 [Homo sapiens]
gi|5803199|ref|NP_006844.1| kallikrein 11 isoform 1 preproprotein [Homo sapiens]
gi|5713131|gb|AAD47815.1| trypsin-like serine protease [Homo sapiens]
gi|18314498|gb|AAH22068.1| Kallikrein 11, isoform 1 preproprotein [Homo sapiens]
gi|11244769|gb|AAG33364.1| keratinocyte trypsin-like serine protease [Homo sapiens
gi|10799396|gb|AAG23257.1| Homo sapiens kallikrein 11
gi|9296987|sp|Q9UBX7|KLK11_HUMAN Kallikrein 11 precursor (Hippostasin) (Trypsin-li
(UNQ649/PRO1279)
gi|6681454|dbj|BAA88713.1| Hippostasin [Homo sapiens]
Length = 250

Score = 221 bits (563), Expect = 1e-56
Identities = 104/249 (41%), Positives = 151/249 (60%), Gaps = 6/249 (2%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M++L L L+    +       + +++ G  C    S P+QAAL+     LLCG   LI P+W+LTA
Sbjct: 1    MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTA 60

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----ETHDNDIMMVHLKNPV 123
            AHC KP    V LG+HNL++ E   ++   +   +  HP +N      + H NDIM+V + +PV
Sbjct: 61   AHCLKPRYIVHLGQHNLQKEEGCEQTRTATESFPHPGFNNSLPNKDHRNDIMLVKMASPV 120

Query: 124  KFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPG 181
             +   ++PL  L + C      +C I GWG    +       P T++CA++ ++   ++CE AYPG
Sbjct: 121  SITWAVRPLTLSSRCVTAGTSCLISGWGSTSSPQLRLPHTLRCANITIIEHQKCENAYPG 180

Query: 182  KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHI 241
             IT +MVCA   + G DSCQGDSGGPLVC    L+G++SWG  PC     KPGVYT VC ++
Sbjct: 181  NITDTMVCASVQEGGKDSCQGDSGGPLVCNQSLQGIISWGQDPCAITRKPGVYTKVCKYV 240

Query: 242  RWIQNILRN 250
             WIQ  ++N
Sbjct: 241  DWIQETMKN 249
```

>gi|21618357|ref|NP_659196.1| kallikrein 11 isoform 2 precursor [Homo sapiens]
gi|3649791|dbj|BAA33404.1| serine protease (TLSP) [Homo sapiens]

```
 gi|8574439|dbj|BAA96797.1|  G  prostate-type hippostasin [Homo sapiens]
          Length = 282

 Score =  221 bits (563), Expect = 1e-56
 Identities = 104/249 (41%), Positives = 151/249 (60%), Gaps = 6/249 (2%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M++L L L+    +      + +++ G  C    S P+QAAL+     LLCG  LI P+W+LTA
Sbjct: 33   MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTA 92

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----ETHDNDIMMVHLKNPV 123
            AHC KP    V LG+HNL++ E  ++   +    +  HP +N     + H NDIM+V + +PV
Sbjct: 93   AHCLKPRYIVHLGQHNLQKEEGCEQTRTATESFPHPGFNNSLPNKDHRNDIMLVKMASPV 152

Query: 124  KFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPG 181
              +   ++PL  L + C      +C I GWG    +       P T++CA++ ++  ++CE AYPG
Sbjct: 153  SITWAVRPLTLSSRCVTAGTSCLISGWGSTSSPQLRLPHTLRCANITIIEHQKCENAYPG 212

Query: 182  KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHI 241
             IT +MVCA    + G DSCQGDSGGPLVC    L+G++SWG   PC     KPGVYT VC ++
Sbjct: 213  NITDTMVCASVQEGGKDSCQGDSGGPLVCNQSLQGIISWGQDPCAITRKPGVYTKVCKYV 272

Query: 242  RWIQNILRN 250
             WIQ   ++N
Sbjct: 273  DWIQETMKN 281


 >gi|51714016|ref|XP_489833.1|  G  similar to trypsinogen 12 [Mus musculus]
 gi|2358116|gb|AAB69086.1|     trypsinogen 12 [Mus musculus]
          Length = 245

 Score =  221 bits (562), Expect = 2e-56
 Identities = 106/241 (43%), Positives = 156/241 (64%), Gaps = 4/241 (1%)

Query: 10   MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            +L L LV A  A+   + +K+V G  C ++S P+Q +L   SG+  CGG LI+ QWV++AAH
Sbjct: 4    LLFLALVGAAVAFPVDDDKIVGGYTCRENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAH 62

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C K   +QV LG+HN++   E   ++ ++   + I HP +N +T +NDIM++ L +PV  + ++
Sbjct: 63   CYKTRIQVRLGEHNIKVLEGNEQFVNAAKIIKHPNFNRKTLNNDIMLIKLSSPVTLNARV 122

Query: 130  QPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQSM 187
             + L + C+      C I GWG   +      PD +QC D   L+P++  CE +YPGKIT +M
Sbjct: 123  ATVALPSSCAPAGTQCLISGWGNTLSFGVSEPDLLQCLDAPLLPQADCEASYPGKITGNM 182

Query: 188  VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
            VCAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 183  VCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALADNPGVYTKVCNYVDWIQDT 241

Query: 248  L 248
            +
Sbjct: 242  I 242


 >gi|6678439|ref|NP_033456.1|  G  protease, serine, 2 [Mus musculus]
 gi|2358119|gb|AAB69089.1|  G  trypsinogen 20 [Mus musculus]
```

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gi|4239961|dbj|BAA74759.1|  G pancreatic trypsin [Mus musculus]
gi|91854|pir||B25528   trypsin (EC 3.4.21.4) precursor - mouse
gi|54919|emb|CAA28243.1|  G unnamed protein product [Mus musculus]
gi|136428|sp|P07146|TRY2_MOUSE  G Anionic trypsin II precursor (Pretrypsinogen II)
gi|12833518|dbj|BAB22554.1|  G unnamed protein product [Mus musculus]
          Length = 246

 Score =  220 bits (560), Expect = 3e-56
 Identities = 107/242 (44%), Positives = 155/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+   ++ +K+V G  C + S P+Q +L   +G+   CGG LI+ QWV++AA
Sbjct: 4    LLILALVGAAVAFPVDDDDKIVGGYTCRESSVPYQVSL-NAGYHFCGGSLINDQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K   +QV LG+HN+   E  ++ +   + I HP YN  T DNDIM++ L +PV  + +
Sbjct: 63   HCYKYRIQVRLGEHNINVLEGNEQFVDSAKIIRHPNYNSWTLDNDIMLIKLASPVTLNAR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  +PL + C+      C I GWG  + NG + PD +QC D  ++P+  CE +YPG IT +
Sbjct: 123  VASVPLPSSCAPAGTQCLISGWGNTLSNGVNNPDLLQCVDAPVLPQADCEASYPGDITNN 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVVYTDVCTHIRWIQN 246
            M+C G ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQN
Sbjct: 183  MICVGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCAQPDAPGVVYTKVCNYVDWIQN 241

Query: 247  IL 248
              +
Sbjct: 242  TI 243


>gi|57036282|ref|XP_533604.1|  G PREDICTED: similar to kallikrein 11 isoform 2 preci
            familiaris]
          Length = 554

 Score =  220 bits (560), Expect = 3e-56
 Identities = 101/254 (39%), Positives = 152/254 (59%), Gaps = 9/254 (3%)

Query: 3    MKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQ 62
            M M+ ++++    LV    +      + +++ G  C   S P+Q AL+     LLCG  LI P+
Sbjct: 303  MAMMILRLIMFALV---TGHVRAETRIIKGYECSPHSQPWQVALFQKTRLLCGATLIAPK 359

Query: 63   WVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----ETHDNDIMMVH 118
            W+LTAAHC+KP   V LG+HNL++ +  ++ +S   +  HP +N    + H NDIM+V
Sbjct: 360  WLLTAAHCRKPRYVVHLGEHNLQRRDGCEQTLSATESFPHPDFNNSLPNKDHRNDIMLVK 419

Query: 119  LKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCE 176
            +     +  ++PL L + C      C + GWG   +    P T++CA++ ++   E+CE
Sbjct: 420  MTRAAFITWAVRPLTLSSHCVTPGTRCLVSGWGSTSSPQLQLPHTLRCANITIINHEECE 479

Query: 177  RAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVVYTD 236
            +AYPG IT +MVCA  ++ G DSCQGDSGGPLVC G L+G++SWG  PC    KPGVYT
Sbjct: 480  KAYPGNITNTMVCASVLESGKDSCQGDSGGPLVCDGSLQGIISWGQDPCAVTRKPGVYTK 539

Query: 237  VCTHIRWIQNILRN 250
            VC ++ WI+  + N
Sbjct: 540  VCKYVDWIRKTMEN 553
```

```
 Score =  209 bits (531), Expect = 7e-53
 Identities = 108/250 (43%), Positives = 145/250 (58%), Gaps = 7/250 (2%)

Query: 1    MPMKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID 60
            M   + +T+     L L               EK+V G  C + S P+Q  L+    +L CGGVLID
Sbjct: 55   MTWRWVTLGSSILLLFCVTGLSQPATEKIVKGKECARHSQPWQVGLFEGANLRCGGVLID 114

Query: 61   PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN--PETHDNDIMMVH 118
             +WVLTAAHC        V LG+H+L + +  ++        ++ HP Y      +HDNDI ++
Sbjct: 115  RRWVLTAAHC-SGRYWVRLGEHSLSRLDWTEKIRRSGFSMTHPSYQGAQHSHDNDIRLLR 173

Query: 119  LKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCE 176
            L   PV   ++ IQPLPL    C+        CQI GWG          FPD +QC +V +V     C
Sbjct: 174  LGTPVPLTRSIQPLPLPTTCAVAGTKCQISGWGITNQLWNPFPDLLQCLNVSIVSSAACR 233

Query: 177  RAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDM-PCGSKEKPGVYT 235
              +PG+IT +MVCA     EG D+CQGDSGGPLVCG  L+GLVSWG + PCG K   PGVYT
Sbjct: 234  AVFPGRITDNMVCASG-TEGADACQGDSGGPLVCGNVLQGLVSWGTVEPCGQKGIPGVYT 292

Query: 236  DVCTHIRWIQ 245
            ++C ++ WI+
Sbjct: 293  NICKYVDWIR 302
```

>gi|58257843|gb|AAW69362.1| try9 [Macaca mulatta]
Length = 247

```
 Score =  219 bits (559), Expect = 4e-56
 Identities = 104/227 (45%), Positives = 141/227 (62%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q  LY SG+  CGG LI  QWV++A HC KP +QVILG+HN
Sbjct: 19   DDDDKIVGGYTCKENSVPYQVFLY-SGYHFCGGALICEQWVISACHCYKPRIQVILGEHN 77

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +   E  ++ IS D+ I HP YNP T DNDIM++ L   P    +  + +PL
Sbjct: 78   INVLEGTEQFISADKIICHPEYNPTTLDNDIMLIKLSTPAIINDYVSIIPLPTHPPVPCT 137

Query: 144  NCQILGWGK--MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG        D+PD +QC D  ++ + +CE  YPG+IT +M C G ++ G DSCQ
Sbjct: 138  ECLISGWGNTLSYGADYPDELQCLDAPVLTQAECEACYPGRITSNMFCIGFLEGGKDSCQ 197

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP VC G L+G+VSWGD  C  K KPGVYT V ++ WI+ +
Sbjct: 198  GDSGGPAVCDGELQGIVSWGD-GCAQKNKPGVYTKVHNYLAWIKETI 243
```

>gi|6981420|ref|NP_036767.1| G pancreatic trypsin 1 [Rattus norvegicus]
gi|57408|emb|CAA24580.1| G unnamed protein product [Rattus norvegicus]
gi|67547|pir||TRRT1 trypsin (EC 3.4.21.4) I precursor - rat
gi|136409|sp|P00762|TRY1_RAT G Anionic trypsin I precursor (Pretrypsinogen I)
gi|206508|gb|AAA98518.1| G trypsinogen I
Length = 246

```
 Score =  219 bits (558), Expect = 5e-56
 Identities = 109/242 (45%), Positives = 157/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  E+ +K+V G  C + S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4    LLILALVGAAVAFPLEDDDKIVGGYTCPEHSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ I+  + I HP Y+  T +NDIM++ L +PVK + +
Sbjct: 63   HCYKSRIQVRLGEHNINVLEGDEQFINAAKIIKHPNYSSWTLNNDIMLIKLSSPVKLNAR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
            + P+ L + C+     C I GWG  + NG + PD +QC D  ++ +  CE AYPG+IT S
Sbjct: 123  VAPVALPSACAPAGTQCLISGWGNTLSNGVNNPDLLQCVDAPVLSQADCEAAYPGEITSS 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M+C G ++ G DSCQGDSGGP+VC G+L+G+VSWG   C     PGVYT VC   + WIQ+
Sbjct: 183  MICVGFLEGGKDSCQGDSGGPVVCNGQLQGIVSWG-YGCALPDNPGVYTKVCNFVGWIQD 241

Query: 247  IL 248
             +
Sbjct: 242  TI 243
```

>gi|6755893|ref|NP_035776.1| trypsin 4 [Mus musculus]
gi|2358085|gb|AAB69056.1| trypsinogen 8 [Mus musculus]
gi|38511693|gb|AAH61135.1| Trypsin 4 [Mus musculus]
gi|4239965|dbj|BAA74761.1| pancreatic trypsin [Mus musculus]
gi|12843002|dbj|BAB25821.1| unnamed protein product [Mus musculus]
gi|12833488|dbj|BAB22542.1| unnamed protein product [Mus musculus]
Length = 246

```
 Score =  219 bits (558), Expect = 5e-56
 Identities = 106/242 (43%), Positives = 157/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4    LLFLALVGAAVAFPVDDDDKIVGGYTCRENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ ++  + I HP +N  T +NDIM++ L +PV  + +
Sbjct: 63   HCYKSRIQVRLGEHNINVLEGNEQFVNSAKIIKHPNFNSRTLNNDIMLIKLASPVTLNAR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+     C I GWG  +    + PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 123  VATVALPSSCAPAGTQCLISGWGNTLSFGVNNPDLLQCLDAPLLPQADCEASYPGKITNN 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M+C G ++ G DSCQGDSGGP+VC G+L+G+VSWG   C  K+ PGVYT VC ++ WIQN
Sbjct: 183  MICVGFLEGGKDSCQGDSGGPVVCNGQLQGIVSWG-YGCALKDNPGVYTKVCNYVDWIQN 241

Query: 247  IL 248
             +
Sbjct: 242  TI 243
```

```
>gi|67548|pir||TRRT2   trypsin (EC 3.4.21.4) II precursor - rat
          Length = 246

 Score =  218 bits (556), Expect = 9e-56
 Identities = 107/242 (44%), Positives = 159/242 (65%), Gaps = 5/242 (2%)

Query: 10  MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4   LLFLALVGAAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ I+  + I HP ++ +T +NDIM++ L +PVK + +
Sbjct: 63  HCYKSRIQVRLGEHNINVLEGDEQFINAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNAR 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +   + L + C+     C I GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 123 VATVALPSSCAPAGTQCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDN 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVC G ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 183 MVCVGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 241

Query: 247 IL 248
             +
Sbjct: 242 TI 243


>gi|6981422|ref|NP_036861.1|  protease, serine, 2 [Rattus norvegicus]
 gi|206506|gb|AAA98517.1|  trypsinogen II [Rattus norvegicus]
 gi|2851507|sp|P00763|TRY2_RAT  Anionic trypsin II precursor (Pretrypsinogen II)
          Length = 246

 Score =  218 bits (555), Expect = 1e-55
 Identities = 106/242 (43%), Positives = 159/242 (65%), Gaps = 5/242 (2%)

Query: 10  MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4   LLFLALVGAAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ ++  + I HP ++ +T +NDIM++ L +PVK + +
Sbjct: 63  HCYKSRIQVRLGEHNINVLEGNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNAR 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +   + L + C+     C I GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 123 VATVALPSSCAPAGTQCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDN 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVC G ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 183 MVCVGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 241

Query: 247 IL 248
             +
Sbjct: 242 TI 243
```

```
>gi|47206216|emb|CAF90862.1|   unnamed protein product [Tetraodon nigroviridis]
          Length = 240

 Score =  218 bits (554), Expect = 2e-55
 Identities = 100/230 (43%), Positives = 151/230 (65%), Gaps = 7/230 (3%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCK-KPNLQVILGKH 82
             ++  K+V G   CLK+S P+Q +L+T G+   CGG+L+   +WVL+AAHCK K +++V LG+H
Sbjct: 11   KDDNKIVGGYECLKNSVPYQVSLFT-GYNFCGGILLSAEWVLSAAHCKPKSDVEVRLGEH 69

Query: 83   NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
             ++ + +   ++ I     + I HP YNP T D+DIM++ L   P    +   + P   L + C+ +
Sbjct: 70   DIWEPDGTEQHIMSSQFIRHPDYNPRTQDSDIMLIKLSRPATLNSFVSPAALPSRCAADG 129

Query: 143  PNCQILGWGKMENGD----FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGND 198
              CQI GWG +    D     +PD +QC +   L+   + C   AYP +IT++M+CAG ++ G D
Sbjct: 130  TMCQISGWGSLRPSDEGSRYPDKLQCLEAPLLSDDTCFNAYPFQITKNMICAGYLEGGKD 189

Query: 199  SCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             SCQGDSGGPL+C G L+G+VSWG   C   + KPGVYT VC +I WI++ +
Sbjct: 190  SCQGDSGGPLMCNGELQGVVSWGH-GCAQRNKPGVYTKVCNYISWIKDTM 238


>gi|51010909|ref|NP_001003405.1|  G RIKEN cDNA 1810049H19 gene [Mus musculus]
 gi|2358086|gb|AAB69057.1|  G trypsinogen 9 [Mus musculus]
 gi|4239963|dbj|BAA74760.1|  G TESP4 [Mus musculus]
 gi|6016832|dbj|BAA85187.1|  G TESP4 [Mus musculus]
 gi|12841657|dbj|BAB25300.1|  G unnamed protein product [Mus musculus]
          Length = 246

 Score =  217 bits (553), Expect = 2e-55
 Identities = 105/242 (43%), Positives = 157/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
             +L L LV A   A+   ++ +K+V G   C ++S P+Q +L   SG+   CGG LI+ QWV++AA
Sbjct: 4    LLFLALVGAAVAFPVDDDDKIVGGYTCRENSIPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
             HC K  +QV LG+HN+   E  ++ ++  + I HP +N  T +NDIM++ L +PV  + +
Sbjct: 63   HCYKTRIQVRLGEHNINVLEGNEQFVNSAKIIKHPNFNSRTLNNDIMLIKLASPVTLNAR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQS 186
             +  + L + C+     C I GWG   +     + PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 123  VATVALPSSCAPAGTQCLISGWGNTLSFGVNNPDLLQCLDAPLLPQADCEASYPGKITNN 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
             M+C G ++ G DSCQGDSGGP+VC G+L+G+VSWG   C   K+ PGVYT VC ++ WIQ+
Sbjct: 183  MICVGFLEGGKDSCQGDSGGPVVCNGQLQGIVSWG-YGCALKDNPGVYTKVCNYVDWIQD 241

Query: 247  IL 248
              +
Sbjct: 242  TI 243


>gi|16716569|ref|NP_444473.1|  G trypsinogen 16 [Mus musculus]
```

gi|2358118|gb|AAB69088.1| trypsinogen 16 [Mus musculus]
gi|3916748|gb|AAC79093.1| trypsinogen 16 [Mus musculus]
Length = 246

```
 Score =  217 bits (552), Expect = 3e-55
 Identities = 107/242 (44%), Positives = 155/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4    LLFLALVGAAVAFPVDDDDKIVGGYTCRENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ I   + I HP +N +T +NDIM++ L +PV  + +
Sbjct: 63   HCYKTRIQVRLGEHNINVLEGNEQFIDAAKIIKHPNFNRKTLNNDIMLIKLSSPVTLNAR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+      C I GWG    +     PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 123  VATVALPSSCAPAGTQCLISGWGNTLSFGVSEPDLLQCLDAPLLPQADCEASYPGKITGN 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVCAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 183  MVCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 241

Query: 247  IL 248
             +
Sbjct: 242  TI 243
```

>gi|28373261|pdb|1CO7|E Chain E, R117h Mutant Rat Anionic Trypsin Complexed With Pancreatic Trypsin Inhibitor (Bpti)
Length = 245

```
 Score =  217 bits (552), Expect = 3e-55
 Identities = 106/242 (43%), Positives = 158/242 (65%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 3    LLFLALVGAAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 61

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ ++  + I HP ++ +T +NDIM++ L +PVK +
Sbjct: 62   HCYKSRIQVRLGEHNINVLEGNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNAH 121

Query: 129  IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+      C I GWG   +G + PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 122  VATVALPSSCAPAGTQCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDN 181

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVC G ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 182  MVCVGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 240

Query: 247  IL 248
             +
Sbjct: 241  TI 242
```

>gi|51871601|ref|NP_001004097.1| trypsin 10 precursor [Rattus norvegicus]

```
gi|47169490|tpe|CAE48382.1|  G  TPA: trypsin 10 [Rattus norvegicus]
         Length = 246

 Score =  216 bits (551), Expect = 3e-55
 Identities = 106/242 (43%), Positives = 157/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAW-SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+ + + +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4    VLILALVGAAVAFPAADDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINEQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ ++  + I HP +  +T +NDIM++ L +PVK + +
Sbjct: 63   HCYKSRIQVRLGEHNINVLEGNEQFVNAAKIIKHPNFIRKTLNNDIMLIKLSSPVKLNSR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+     C I GWG  +    + PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 123  VATVALPSSCAPAGTQCLISGWGNTLSFGVNEPDLLQCLDAPLLPQADCEASYPGKITDN 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVCAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 183  MVCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 241

Query: 247  IL 248
             +
Sbjct: 242  TI 243


[ ]>gi|2358117|gb|AAB69087.1|   trypsinogen 15 [Mus musculus]
         Length = 246

 Score =  216 bits (551), Expect = 3e-55
 Identities = 106/241 (43%), Positives = 155/241 (64%), Gaps = 5/241 (2%)

Query: 11   LALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAH
Sbjct: 5    LILALVGAAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAH 63

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C K  +QV LG+HN+   E  ++ ++  + I HP +N +T +NDIM++ L +PV  + ++
Sbjct: 64   CYKTRIQVRLGEHNINVLEGNEQFVNAAKIIKHPNFNRKTLNNDIMLIKLSSPVTLNARV 123

Query: 130  QPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQSM 187
              + L + C+     C I GWG  +      PD +QC D  L+P+  CE +YPGKIT +M
Sbjct: 124  ATVALPSSCAPAGTQCLISGWGNTLSFGVSEPDLLQCLDAPLLPQADCEASYPGKITGNM 183

Query: 188  VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
            VCAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 184  VCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDT 242

Query: 248  L 248
            +
Sbjct: 243  I 243


[ ]>gi|758266|emb|CAA24581.1|  G  unnamed protein product [Rattus norvegicus]
         Length = 238
```

```
 Score =  216 bits (550), Expect = 5e-55
 Identities = 100/227 (44%), Positives = 151/227 (66%), Gaps = 4/227 (1%)

Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L  SG+   CGG LI+ QWV++AAHC K  +QV LG+HN
Sbjct: 11  DDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHN 69

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +   E  ++ ++  + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+
Sbjct: 70  INVLEGNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGT 129

Query: 144 NCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQ
Sbjct: 130 QCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQ 189

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+VC G L+G+VSWG   C   + PGVYT VC ++ WIQ+ +
Sbjct: 190 GDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 235
```

>gi|34855584|ref|XP_342669.1| G similar to trypsinogen 9 [Rattus norvegicus]
Length = 246

```
 Score =  216 bits (550), Expect = 5e-55
 Identities = 103/242 (42%), Positives = 156/242 (64%), Gaps = 5/242 (2%)

Query: 10  MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV     A+   ++ +K+V G  C ++S P+Q +L  SG+   CGG LI+ QWV++AA
Sbjct: 4   LLFLALVGVAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ ++  + I HP +N     +NDIM++ L +PVK + +
Sbjct: 63  HCYKTRIQVRLGEHNINVLEGDEQFVNAAKIIKHPNFNARNLNNDIMLIKLSSPVKLNAR 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+      C I GWG   +    + PD +QC D  ++P+  CE +YPGKIT +
Sbjct: 123 VATVALPSSCAPAGTQCLISGWGNTLSLGVNNPDLLQCLDAPVLPQADCEASYPGKITNN 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M+C G ++ G DSCQGDSGGP+VC G+L+G+VSWG   C  K+ PGVYT VC ++ WIQ+
Sbjct: 183 MICVGFLEGGKDSCQGDSGGPVVCNGQLQGIVSWG-YGCALKDNPGVYTKVCNYVDWIQD 241

Query: 247 IL 248
             +
Sbjct: 242 TI 243
```

>gi|34855588|ref|XP_342672.1| G similar to trypsin (EC 3.4.21.4) II precursor - rat
norvegicus]
Length = 291

```
 Score =  216 bits (549), Expect = 6e-55
 Identities = 106/250 (42%), Positives = 159/250 (63%), Gaps = 5/250 (2%)

Query: 2   PMKMLTMKMLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID 60
            P + L   +L    LV  + A+   ++ +K+V G  C + S P+Q +L  SG+   CGG LI+
Sbjct: 41  PSRTLKDCLLNHLLVFIQVAFPVDDDDKIVGGYTCQEHSVPYQVSL-NSGYHYCGGSLIN 99
```

```
Query: 61   PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
             QWV++AAHC K   +QV LG+HN+   E   ++ ++   + I HP ++ +T +NDIM++ L
Sbjct: 100  DQWVVSAAHCYKSRIQVRLGEHNINVLEGDEQFVNAAKIIKHPNFDRKTLNNDIMLIKLS 159

Query: 121  NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERA 178
            +PVK + ++   + L + C+        C I GWG   +     + PD +QC D   L+P+   CE +
Sbjct: 160  SPVKLNARVATVALPSSCAPAGTQCLISGWGNTLSFGVNDPDLLQCLDAPLLPQADCEAS 219

Query: 179  YPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVC 238
            YPGKIT +MVCAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC
Sbjct: 220  YPGKITNNMVCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVC 278

Query: 239  THIRWIQNIL 248
             ++ WIQ+ +
Sbjct: 279  NYVDWIQDTI 288
```

>gi|56541274|gb|AAH87610.1| G Hypothetical LOC496627 [Xenopus tropicalis]
gi|58332100|ref|NP_001011202.1| G hypothetical LOC496627 [Xenopus tropicalis]
Length = 243

Score = 216 bits (549), Expect = 6e-55
Identities = 100/243 (41%), Positives = 155/243 (63%), Gaps = 5/243 (2%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK+L +C++L  +A + + +K++ G  C ++S P+  +L  SG+  CGG LI  QWV++A
Sbjct: 1    MKLLLICVLLGAAA-AFDDDKIIGGSTCARNSVPYIVSL-NSGYHFCGGSLISNQWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K ++QV LG+HN+  +E  ++ I+  + I HP YN  T DNDIM++ L +P   +
Sbjct: 59   AHCYKASVQVRLGEHNIALSEGTEQFINSAKVIRHPSYNSRTIDNDIMLIKLASPASLNS 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLVPREQCERAYPGKITQ 185
             +  + L + C+   +C + GWG +     ++PD +QC +  ++   QC  AYPG+IT
Sbjct: 119  AVNTVALPSSCAAAGTSCLVSGWGNLSTTTSNYPDLLQCLNAPILTTAQCSGAYPGQITN 178

Query: 186  SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            +M CAG ++ G DSCQGDSGGP+VC G L+G+VSWG + C  +  PGVY  VC +  WIQ
Sbjct: 179  NMFCAGFLEGGKDSCQGDSGGPVVCNGELQGVVSWG-IGCAQRNYPGVYAKVCNYNSWIQ 237

Query: 246  NIL 248
            + +
Sbjct: 238  STI 240
```

>gi|51711962|ref|XP_487918.1| G PREDICTED: similar to trypsinogen 9 [Mus musculus]
Length = 264

Score = 215 bits (548), Expect = 8e-55
Identities = 99/227 (43%), Positives = 149/227 (65%), Gaps = 4/227 (1%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN
Sbjct: 37   DDDDKIVGGYTCRENSIPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKTRIQVRLGEHN 95

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
```

```
             +    E   ++  ++   + I  HP  +N   T  +NDIM++  L  +PV   +  ++   + L  + C+
Sbjct: 96   INVLEGNEQFVNSAKIIKHPNFNSRTLNNDIMLIKLASPVTLNARVATVALPSSCAPAGT 155

Query: 144  NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG    +    + PD +QC D  L+P+   CE +YPGKIT +M+C G ++ G DSCQ
Sbjct: 156  QCLISGWGNTLSFGVNNPDLLQCLDAPLLPQADCEASYPGKITNNMICVGFLEGGKDSCQ 215

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG    C  K+ PGVYT VC ++ WIQ+ +
Sbjct: 216  GDSGGPVVCNGQLQGIVSWG-YGCALKDNPGVYTKVCNYVDWIQDTI 261
```

>gi|27573668|pdb|1J14|A Chain A, Benzamidine In Complex With Rat Trypsin Mutant X
gi|10120746|pdb|1QL9|A Chain A, Factor Xa Specific Inhibitor In Complex With Rat T
Mutant X99rt
Length = 223

Score = 215 bits (548), Expect = 8e-55
Identities = 100/222 (45%), Positives = 148/222 (66%), Gaps = 4/222 (1%)

```
Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
               ++ ++   + I HP ++ ET++NDIM++ L +PVK + ++   + L + C+     C I
Sbjct: 60   GNEQFVNAAKIIKHPNFDRETYNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149  GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
             GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120  GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             P+VC G L+G+VSWG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 180  PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

>gi|4139560|pdb|3TGJ|E Chain E, S195a Trypsinogen Complexed With Bovine Pancreat:
Inhibitor (Bpti)
Length = 233

Score = 215 bits (547), Expect = 1e-54
Identities = 99/227 (43%), Positives = 151/227 (66%), Gaps = 4/227 (1%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN
Sbjct: 6    DDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHN 64

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +    E   ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+
Sbjct: 65   INVLEGNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGT 124

Query: 144  NCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG  + +G + PD +QC D  L+P+   CE +YPGKIT +MVC G ++ G DSCQ
Sbjct: 125  QCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQ 184

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
```

```
Query: 143 PNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
             C + GWG    +   G +P   +QC +   ++     C+++YPG+IT +M C G ++ G DSC
Sbjct: 138 AQCLVSGWGNTVSIGGKYPALLQCLEAPVLSASSCKKSYPGQITSNMFCLGFLEGGKDSC 197

Query: 201 QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            GDSGGP+VC G ++G+VSWG + C   + KPGVYT VC ++ WIQ  + N
Sbjct: 198 DGDSGGPVVCNGEIQGIVSWGSV-CAMRGKPGVYTKVCNYLSWIQETMAN 246
```

>gi|50054435|ref|NP_001001911.1| kallikrein 1, renal/pancreas/salivary [Sus scro
gi|33637119|gb|AAQ23716.1| glandular kallikrein precursor [Sus scrofa]
Length = 263

Score = 211 bits (536), Expect = 2e-53
Identities = 98/238 (41%), Positives = 140/238 (58%), Gaps = 15/238 (6%)

```
Query: 26  QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
           Q +++ G   C KDSHP+Q A+Y       CGGVL+DP+WVLTAAHCK  N QV LG+HNL
Sbjct: 22  QSRIIGGRECEKDSHPWQVAIYHYSSFQCGGVLVDPKWVLTAAHCKNDNYQVWLGRHNLF 81

Query: 86  QTETFQRQISVDRTIVHPRYN-----------PETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           + E    +   V      HP +N              + + +D+M++ L++P K +  ++ L L
Sbjct: 82  ENEVTAQFFGVTADFPHPGFNLSLLKNHTKADGKDYSHDLMLLRLQSPAKITDAVKVLEL 141

Query: 135 KNDCSEENPNCQILGWGKMENG----DFPDTIQCADVHLVPREQCERAYPGKITQSMVCA 190
                 E     CQ   GWG +E G     +FPD IQC ++ L+      C   A+P K+T+SM+CA
Sbjct: 142 PTQEPELGSTCQASGWGSIEPGPDDFEFPDEIQCVELTLLQNTFCADAHPDKVTESMLCA 201

Query: 191 GDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           G +   G D+C GDSGGPL+C G   +G+ SWG   PCGS   KP +YT +  ++ WI + +
Sbjct: 202 GYLPGGKDTCMGDSGGPLICNGMWQGITSWGHTPCGSANKPSIYTKLIFYLDWINDTI 259
```

>gi|27819626|ref|NP_777115.1| pancreatic anionic trypsinogen [Bos taurus]
gi|20302852|gb|AAM18909.1| pancreatic anionic trypsinogen [Bos taurus]
Length = 247

Score = 211 bits (536), Expect = 2e-53
Identities = 102/242 (42%), Positives = 157/242 (64%), Gaps = 5/242 (2%)

```
Query: 10  MLALCLVLAKSAW-SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
           +L L   V A   A+ S++ +K+V G   C ++S P+Q +L   +G+   CGG LI+ QWV++AA
Sbjct: 4   LLILAFVGAAVAFPSDDDDKIVGGYTCAENSVPYQVSL-NAGYHFCGGSLINDQWVVSAA 62

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
           HC + ++QV LG++N+    E   ++ I    + I HP+Y+   T DNDI+++ L   P    + +
Sbjct: 63  HCYQYHIQVRLGEYNIDVLEGGEQFIDASKIIRHPKYSSWTLDNDILLIKLSTPAVINAR 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
           +   L L + C+   +   C I GWG   + +G ++PD +QC +   L+     CE +YPG+IT +
Sbjct: 123 VSTLALPSACASGSTECLISGWGNTLSSGVNYPDLLQCLEAPLLSHADCEASYPGEITNN 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
           M+CAG ++ G DSCQGDSGGP+ C G+L+G+VSWG   C   K KPGVYT VC ++ WIQ
Sbjct: 183 MICAGFLEGGKDSCQGDSGGPVACNGQLQGIVSWG-YGCAQKGKPGVYTKVCNYVDWIQE 241
```

```
 Identities = 97/227 (42%), Positives = 143/227 (62%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G   C   ++ P+Q +L   SG+   CGG LI+ QWV++AAHC K   +QV LG+ N
Sbjct: 2    DDDDKIVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDN 60

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +    E   ++ IS   ++IVHP YN   T +NDIM++ LK+      + ++   + L    C+
Sbjct: 61   INVVEGNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGT 120

Query: 144  NCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG   K       +PD ++C      ++      C+ AYPG+IT +M CAG ++ G DSCQ
Sbjct: 121  QCLISGWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQ 180

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG    C   K KPGVYT VC ++ WI+  +
Sbjct: 181  GDSGGPVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 226
```

>gi|17942679|pdb|1K9O|E Chain E, Crystal Structure Of Michaelis Serpin-Trypsin Co
Length = 223

```
 Score =  211 bits (536), Expect = 2e-53
 Identities = 98/222 (44%), Positives = 147/222 (66%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G   C ++S P+Q +L   SG+   CGG LI+ QWV++AAHC K   +QV LG+HN+    E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
               ++ ++    + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+      C I
Sbjct: 60   GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149  GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
             GWG   + +G + PD +QC D  L+P+   CE +YPGKIT +MVC G ++ G DSCQGD+GG
Sbjct: 120  GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDAGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             P+VC G L+G+VSWG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 180  PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

>gi|2358083|gb|AAB69055.1| trypsinogen 4 [Mus musculus]
gi|12963793|ref|NP_076196.1| RIKEN cDNA 1810009J06 [Mus musculus]
gi|12840938|dbj|BAB25018.1| unnamed protein product [Mus musculus]
Length = 247

```
 Score =  211 bits (536), Expect = 2e-53
 Identities = 97/230 (42%), Positives = 141/230 (61%), Gaps = 3/230 (1%)

Query: 23   SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKH 82
             +    +K+V G   C K S P+Q +L         CGG LI  QWVL+AAHC K   LQV LG+H
Sbjct: 18   ANSDDKIVGGYTCPKHSVPYQVSLNDGISHQCGGSLISDQWVLSAAHCYKRRLQVRLGEH 77

Query: 83   NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
             N+    E   ++ I   ++ I HP YN +T DNDIM++ LK+P     + ++   + L    C+  N
Sbjct: 78   NIDVLEGGEQFIDAEKIIRHPDYNKDTVDNDIMLIKLKSPAILNSQVSTVSLPRSCASTN 137
```

```
          Copper (Ii) Chelate
gi|13096614|pdb|1G3D|A  Chain A, Bovine Beta-Trypsin Bound To Meta-Amidino Schiff B
          Copper (Ii) Chelate
gi|13096613|pdb|1G3C|A  Chain A, Bovine Beta-Trypsin Bound To Para-Amidino Schiff B
          Iron(Iii) Chelate
gi|13096612|pdb|1G3B|A  Chain A, Bovine Beta-Trypsin Bound To Meta-Amidino Schiff B
          Magnesium(Ii) Chelate
         Length = 228

 Score =  211 bits (538), Expect = 1e-53
 Identities = 97/227 (42%), Positives = 143/227 (62%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C  ++ P+Q +L  SG+   CGG LI+ QWV++AAHC K   +QV LG+ N
Sbjct: 1    DDDDKIVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDN 59

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +    E  ++ IS  ++IVHP YN  T +NDIM++ LK+     + ++  + L    C+
Sbjct: 60   INVVEGNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGT 119

Query: 144  NCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG  K      +PD ++C      ++     C+ AYPG+IT +M CAG ++ G DSCQ
Sbjct: 120  QCLISGWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQ 179

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG    C  K KPGVYT VC ++ WI+  +
Sbjct: 180  GDSGGPVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 225


>gi|5542503|pdb|1ZZZ|A  Chain A, Trypsin Inhibitors With Rigid Tripeptidyl Aldehy
         Length = 237

 Score =  211 bits (538), Expect = 1e-53
 Identities = 97/227 (42%), Positives = 143/227 (62%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C  ++ P+Q +L  SG+   CGG LI+ QWV++AAHC K   +QV LG+ N
Sbjct: 10   DDDDKIVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDN 68

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +    E  ++ IS  ++IVHP YN  T +NDIM++ LK+     + ++  + L    C+
Sbjct: 69   INVVEGNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGT 128

Query: 144  NCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG  K      +PD ++C      ++     C+ AYPG+IT +M CAG ++ G DSCQ
Sbjct: 129  QCLISGWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQ 188

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG    C  K KPGVYT VC ++ WI+  +
Sbjct: 189  GDSGGPVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 234


>gi|1421532|pdb|1TGB|  Trypsinogen-Ca From Peg
         Length = 229

 Score =  211 bits (538), Expect = 1e-53
```

gi|809461|pdb|1TNJ| Trypsin (E.C.3.4.21.4) Complexed With The Inhibitor 2-Phenylethylamine

gi|809460|pdb|1TNI| Trypsin (E.C.3.4.21.4) Complexed With The Inhibitor 4-Phenylbutylamine

gi|809459|pdb|1TNH| Trypsin (E.C.3.4.21.4) Complexed With The Inhibitor 4-Fluorobenzylamine

gi|809458|pdb|1TNG| Trypsin (E.C.3.4.21.4) Complexed With The Inhibitor Aminomethylcyclohexane

gi|230352|pdb|1TGT| Trypsinogen (173 Degrees K, 0.70 Methanol, 0.30 Water)

gi|230350|pdb|1TGS|Z Chain Z, Trypsinogen Complex With Porcine Pancreatic Secretor Trypsin Inhibitor

gi|230349|pdb|1TGN| Trypsinogen

gi|230347|pdb|1TGC| Trypsinogen (0.50 Methanol, 0.50 Water)

gi|1311387|pdb|1BTZ|A Chain A, Tripeptideboronate Methyl Ester Inhibited Mol_id: 1 Molecule: Beta-Trypsin; Chain: A; Ec: 3.4.21.4; Mol_id: 2; Molecule: T-Butoxy-Ala-Val-Boro-Lys Methyl Ester; Chain: H

gi|1311388|pdb|1BTY| Benzamidine Inhibited Mol_id: 1; Molecule: Beta-Trypsin; Cha Null; Ec: 3.4.21.4; Heterogen: Benzamidine

gi|1311389|pdb|1BTX|A Chain A, Tripeptideboronate Ethyl Ester Inhibited Mol_id: 1; Molecule: Beta-Trypsin; Chain: A; Ec: 3.4.21.4; Mol_id: 2; Molecule: T-Butoxy-Ala-Val-Boro-Lys Ethyl Ester; Chain: H

gi|1311391|pdb|1BTW|A Chain A, Tripeptideboronate 1,3-Propanediol Monoester-Inhibi Mol_id: 1; Molecule: Beta-Trypsin; Chain: A; Ec: 3.4.21.4; Mol_id: 2; Molecule: T-Butoxy-Ala-Val-Boro-Lys 1,3-Propanediol Monoester; Chain: H

gi|1310895|pdb|1BTP| Mol_id: 1; Molecule: Beta-Trypsin; Chain: Null; Ec: 3.4.21.4 Heterogen: N-[3-[4-[4-(Amidinophenoxy)-Carbonyl]phenyl]-2-Methyl-2-Propenoyl]-N-Allylglycine Methanesulfonate

Length = 229

Score = 211 bits (538), Expect = 1e-53
Identities = 97/227 (42%), Positives = 143/227 (62%), Gaps = 4/227 (1%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N
Sbjct: 2    DDDDKIVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDN 60

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +   E  ++ IS  ++IVHP YN  T +NDIM++ LK+    + ++  + L   C+
Sbjct: 61   INVVEGNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGT 120

Query: 144 NCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG  K     +PD ++C     ++    C+ AYPG+IT +M CAG ++ G DSCQ
Sbjct: 121 QCLISGWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQ 180

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG   C  K KPGVYT VC ++ WI+  +
Sbjct: 181 GDSGGPVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 226
```

>gi|13096615|pdb|1G3E|A Chain A, Bovine Beta-Trypsin Bound To Para-Amidino Schif

>gi|559311|dbj|BAA07516.1| G pancreas cationic pretrypsinogen [Bos taurus]
gi|2507249|sp|P00760|TRY1_BOVIN Cationic trypsin precursor (Beta-trypsin)
gi|42543839|pdb|1UTQ|A S Chain A, Trypsin Specificity As Elucidated By Lie Calculati
X-Ray Structures And Association Constant Measurements
gi|42543838|pdb|1UTP|A S Chain A, Trypsin Specificity As Elucidated By Lie Calculati
X-Ray Structures And Association Constant Measurements
gi|42543837|pdb|1UTO|A S Chain A, Trypsin Specificity As Elucidated By Lie Calculati
X-Ray Structures And Association Constant Measurements
gi|42543836|pdb|1UTN|A S Chain A, Trypsin Specificity As Elucidated By Lie Calculati
X-Ray Structures And Association Constant Measurements
gi|31615517|pdb|1LQE|A S Chain A, Crystal Structure Of Trypsin In Complex With 79.
gi|11514323|pdb|1EZX|C S Chain C, Crystal Structure Of A Serpin:protease Complex
gi|10835693|pdb|1F0U|A S Chain A, Bovine Trypsin Complexed With Rpr128515
gi|10835692|pdb|1F0T|A S Chain A, Bovine Trypsin Complexed With Rpr131247
Length = 243

Score = 211 bits (538), Expect = 1e-53
Identities = 97/227 (42%), Positives = 143/227 (62%), Gaps = 4/227 (1%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G   C   ++ P+Q +L   SG+   CGG LI+ QWV++AAHC K   +QV LG+ N
Sbjct: 16   DDDDKIVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDN 74

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +    E  ++ IS   ++IVHP YN   T +NDIM++ LK+     + ++  + L    C+
Sbjct: 75   INVVEGNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGT 134

Query: 144  NCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG  K     +PD ++C     ++     C+ AYPG+IT +M CAG ++ G DSCQ
Sbjct: 135  QCLISGWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQ 194

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG     C   K KPGVYT VC ++ WI+   +
Sbjct: 195  GDSGGPVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 240
```

>gi|67549|pir||TRBOTR trypsin (EC 3.4.21.4) precursor - bovine
gi|231094|pdb|4TPI|Z S Chain Z, Trypsinogen Complex With The Arg15-Analogue Of Pancr
Trypsin Inhibitor And Val-Val
gi|230935|pdb|3TPI|Z S Chain Z, Trypsinogen Complex With Pancreatic Trypsin Inhibito
Ile-Val
gi|230773|pdb|2TPI|Z S Chain Z, Trypsinogen - Pancreatic Trypsin Inhibitor - Ile-Val
Complex (2.4 M Magnesium Sulfate)
gi|230764|pdb|2TGT| S Trypsinogen (103 Degrees K, 0.70 Methanol, 0.30 Water)
gi|230762|pdb|2TGP|Z S Chain Z, Trypsinogen Complex With Pancreatic Trypsin Inhibito
gi|230761|pdb|2TGD| S Trypsinogen, Diisopropylphosphoryl Inhibited
gi|230760|pdb|2TGA| S Trypsinogen (2.4 M Magnesium Sulfate)
gi|809463|pdb|1TNL| S Trypsin (E.C.3.4.21.4) Complexed With The Inhibitor Tranylcyp
gi|809462|pdb|1TNK| S Trypsin (E.C.3.4.21.4) Complexed With The Inhibitor
3-Phenylpropylamine

```
Sbjct: 78  IAVSEGGEQFINAAKIIRHPRYNANTIDNDIMLIKLSSPATLNSRVSAIALPKSCPAAGT 137

Query: 144 NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG  ++   ++PD +QC    ++     C  AYPG+I+ +M+C G M+ G DSCQ
Sbjct: 138 QCLISGWGNTQSIGQNYPDVLQCLKAPILSDSVCRNAYPGQISSNMMCLGYMEGGKDSCQ 197

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+VC G L+G+VSWG   C  K KPGVYT VC ++ WIQ  +
Sbjct: 198 GDSGGPVVCNGELQGVVSWG-AGCAQKGKPGVYTRVCKYVSWIQQTI 243
```

>gi|4139558|pdb|3TGI|E Chain E, Wild-Type Rat Anionic Trypsin Complexed With Bov:
Pancreatic Trypsin Inhibitor (Bpti)
gi|2098544|pdb|1ANE| Anionic Trypsin Wild Type
Length = 223

Score = 212 bits (539), Expect = 9e-54
Identities = 99/222 (44%), Positives = 147/222 (66%), Gaps = 4/222 (1%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1   IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+      C I
Sbjct: 60  GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149 GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120 GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 180 PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

>gi|2098543|pdb|1AND| Anionic Trypsin Mutant With Arg 96 Replaced By His
Length = 223

Score = 212 bits (539), Expect = 9e-54
Identities = 99/222 (44%), Positives = 147/222 (66%), Gaps = 4/222 (1%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1   IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+      C I
Sbjct: 60  GNEQFVNAAKIIKHPNFDHKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149 GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120 GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 180 PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN
Sbjct: 19   DDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHN 77

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +   E  ++ ++  + I HP +N    +NDIM++ L  PV  + ++  + L + C+
Sbjct: 78   INVLEGNEQFVNAAKIIKHPNFNARNLNNDIMLIKLSVPVTLNSRVATVALPSSCAPAGT 137

Query: 144  NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG   +   + PD +QC D  ++P+  CE +YPGKIT +M+C G ++ G DSCQ
Sbjct: 138  QCLISGWGNTLSLGVNNPDLLQCLDAPVLPQADCEASYPGKITNNMICVGFLEGGKDSCQ 197

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+VC G+L+G+VSWG   C  K+ PGVYT VC ++ WIQ+ +
Sbjct: 198  GDSGGPVVCNGQLQGIVSWG-YGCALKDNPGVYTKVCNYVDWIQDTI 243
```

>gi|1633121|pdb|1SLX|B Chain B, Rat Anionic N143h, E151h Trypsin Complexed To A86
Zinc-Bound
gi|1633125|pdb|1SLV|B Chain B, Rat Anionic N143h, E151h Trypsin Complexed To A86h
Copper-Bound
gi|1633127|pdb|1SLU|B Chain B, Rat Anionic N143h, E151h Trypsin Complexed To A86h
Length = 223

Score = 212 bits (540), Expect = 7e-54
Identities = 99/222 (44%), Positives = 147/222 (66%), Gaps = 4/222 (1%)

```
Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ ++  + I HP ++ +T +NDIM++ L +PVK + ++  + L + C+      C I
Sbjct: 60   GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149  GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120  GWGHTLSSGVNHPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 180  PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

>gi|57097397|ref|XP_532744.1| PREDICTED: similar to trypsin (EC 3.4.21.4) precurs
dog [Canis familiaris]
Length = 246

Score = 212 bits (539), Expect = 9e-54
Identities = 98/227 (43%), Positives = 144/227 (63%), Gaps = 4/227 (1%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG++N
Sbjct: 19   DDDDKIVGGYTCSRNSVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSRIQVRLGEYN 77

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +  +E  ++ I+  + I HPRYN  T DNDIM++ L +P   + ++  + L   C
```

```
gi|55742601|ref|NP_001007055.1|  G zgc:92590 [Danio rerio]
        Length = 247

 Score =  213 bits (541), Expect = 5e-54
 Identities = 104/248 (41%), Positives = 153/248 (61%), Gaps = 7/248 (2%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAAL-YTSGHLLCGGVLIDPQWVLT 66
            MKM+    L++     A S + +K++ G  C   +S P+Q  L Y +G    CG  LI+ +W ++
Sbjct: 1    MKMIVFALLVLAVACSAD-DKIIGGYECSPNSQPWQIYLTYDNGQRWCGASLINDRWAVS 59

Query: 67   AAHCK--KPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
            AAHC       L V LG+HN+    E   +++I  ++ I HP+YN  T DND M++ LK P
Sbjct: 60   AAHCYLVANRLTVHLGEHNVAVEEGTEQRIKAEKVIPHPKYNDYTLDNDFMLIKLKEPAV 119

Query: 125  FSKKIQPLPLKNDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGK 182
            F++ +QP+PL    CS E    C + GWG + N     +PD +QC ++ ++ R QCE AY   +
Sbjct: 120  FNQYVQPVPLTTSCSSEGEQCLVSGWGNLINTGVVYPDVLQCLNLPVLTRAQCEGAYGWQ 179

Query: 183  ITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
            IT++M CAG M+ G D+CQGDSGGP++C G LRG+VSWG    C       PGVYT+VC +
Sbjct: 180  ITKNMFCAGFMEGGKDACQGDSGGPVICNGELRGVVSWG-YGCADSGYPGVYTEVCRYTD 238

Query: 243  WIQNILRN 250
            W+ + + N
Sbjct: 239  WVASTIAN 246


>gi|1633123|pdb|1SLW|B  S Chain B, Rat Anionic N143h, E151h Trypsin Complexed To A86
            Nickel-Bound
           Length = 223

 Score =  213 bits (541), Expect = 5e-54
 Identities = 99/222 (44%), Positives = 147/222 (66%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++  + L + C+      C I
Sbjct: 60   GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATIALPSSCAPAGTQCLIS 119

Query: 149  GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120  GWGHTLSSGVNHPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+VSWG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 180  PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220


>gi|34855586|ref|XP_342670.1|  G similar to trypsinogen 8 [Rattus norvegicus]
           Length = 246

 Score =  212 bits (540), Expect = 7e-54
 Identities = 97/227 (42%), Positives = 147/227 (64%), Gaps = 4/227 (1%)
```

```
>gi|27731519|ref|XP_218644.1|  G  similar to kallikrein 12 isoform 2; kallikrein-like
          [Rattus norvegicus]
         Length = 247

 Score =  213 bits (542), Expect = 4e-54
 Identities = 103/246 (41%), Positives = 154/246 (62%), Gaps = 10/246 (4%)

Query: 10   MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            +L LC+V    A    ++EK+ +G  C+K+S P+Q  L+    +L CGGVL+D +WVLTAAH
Sbjct: 6    LLLLCVVGLSQA---DREKIYNGVECVKNSQPWQVGLFHGKYLRCGGVLVDRKWVLTAAH 62

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP--ETHDNDIMMVHLKNPVKFSK 127
            C      V LG+H+L + +  ++        +I HP Y+    + H++D+ ++ L  P+  +
Sbjct: 63   C-SGKYMVRLGEHSLSKLDLTEQLRLTTFSITHPSYHGAYQNHEHDLRLLRLNRPISLTY 121

Query: 128  KIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQ 185
              ++P+ L + C+     C I GWG         FPD +QC D+ +V  E C    +PG++T+
Sbjct: 122  AVRPVALPSSCAPTGAKCHISGWGTTNKPWDPFPDRLQCLDLSIVSNETCRAVFPGRVTE 181

Query: 186  SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDM-PCGSKEKPGVYTDVCTHIRWI 244
            +M+CAG   + G D+CQGDSGGPLVCGG L+GLVSWG + PCG K  PGVYT VC +  WI
Sbjct: 182  NMLCAGG-EAGKDACQGDSGGPLVCGGVLQGLVSWGSVGPCGQKGIPGVYTKVCKYTDWI 240

Query: 245  QNILRN 250
            + ++RN
Sbjct: 241  RVVIRN 246


>gi|27465583|ref|NP_775150.1|  G  cationic trypsinogen [Rattus norvegicus]
 gi|92925|pir||A27547   trypsin (EC 3.4.21.4) precursor, cationic - rat
 gi|136417|sp|P08426|TRY3_RAT  G  Cationic trypsin III precursor (Pretrypsinogen III)
 gi|206499|gb|AAA41985.1|  G  trypsinogen (EC 3.4.21.4)
         Length = 247

 Score =  213 bits (541), Expect = 5e-54
 Identities = 98/224 (43%), Positives = 142/224 (63%), Gaps = 4/224 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C K+S P+Q +L   +G+  CGG LI+ QWV++AAHC K  +QV LG+HN
Sbjct: 20   DDDDKIVGGYTCQKNSLPYQVSL-NAGYHFCGGSLINSQWVVSAAHCYKSRIQVRLGEHN 78

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +   E  ++ I   + I HP YN  T DNDIM++ L +P   + ++  + L   C
Sbjct: 79   IDVVEGGEQFIDAAKIIRHPSYNANTFDNDIMLIKLNSPATLNSRVSTVSLPRSCGSSGT 138

Query: 144  NCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C + GWG  + +G ++P  +QC D  ++    C+ +YPGKIT +M C G ++ G DSCQ
Sbjct: 139  KCLVSGWGNTLSSGTNYPSLLQCLDAPVLSDSSCKSSYPGKITSNMFCLGFLEGGKDSCQ 198

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            GDSGGP+VC G+L+G+VSWG    C  K KPGVYT VC ++ WIQ
Sbjct: 199  GDSGGPVVCNGQLQGVVSWG-YGCAQKGKPGVYTKVCNYVNWIQ 241


>gi|54035518|gb|AAH83528.1|  G  Zgc:92590 [Danio rerio]
```

```
>gi|37182171|gb|AAQ88888.1|  KLK12 [Homo sapiens]
 gi|22208987|ref|NP_665901.1|  kallikrein 12 isoform 2 [Homo sapiens]
 gi|6166249|gb|AAD26426.2|  kallikrein-like protein 5 [Homo sapiens]
 gi|11244770|gb|AAG33365.1|  kallikrein-like 5 [Homo sapiens]
 gi|9296989|sp|Q9UKR0|KLK12_HUMAN  Kallikrein 12 precursor (Kallikrein-like protein
          (UNQ669/PRO1303)
         Length = 248

 Score =  213 bits (543), Expect = 3e-54
 Identities = 107/250 (42%), Positives = 154/250 (61%), Gaps = 10/250 (4%)

Query: 6   LTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVL 65
            L++ +L   L L+++A      K+ +G  C ++S P+Q  L+     L CGGVLID +WVL
Sbjct: 3   LSIFLLLCVLGLSQAA----TPKIFNGTECGRNSQPWQVGLFEGTSLRCGGVLIDHRWVL 58

Query: 66  TAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRY--NPETHDNDIMMVHLKNPV 123
            TAAHC       V LG+H+L Q +  ++        ++ HP Y      +H++D+ ++ L+ PV
Sbjct: 59  TAAHCSGSRYWVRLGEHSLSQLDWTEQIRHSGFSVTHPGYLGASTSHEHDLRLLRLRLPV 118

Query: 124 KFSKKIQPLPLKNDCSEENPNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPG 181
            + +  +QPLPL NDC+      C + GWG          FPD +QC ++ +V     C     YPG
Sbjct: 119 RVTSSVQPLPLPNDCATAGTECHVSGWGITNHPRNPFPDLLQCLNLSIVSHATCHGVYPG 178

Query: 182 KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDM-PCGSKEKPGVYTDVCTH 240
            +IT +MVCAG +  G D+CQGDSGGPLVCGG L+GLVSWG + PCG    PGVYT +C +
Sbjct: 179 RITSNMVCAGGV-PGQDACQGDSGGPLVCGGVLQGLVSWGSVGPCGQDGIPGVYTYICKY 237

Query: 241 IRWIQNILRN 250
            + WI+ I+RN
Sbjct: 238 VDWIRMIMRN 247


>gi|64388|emb|CAA49679.1|   trypsin III [Salmo salar]
 gi|422585|pir||S31779   trypsin (EC 3.4.21.4) III precursor - Atlantic salmon  (fragme
 gi|464949|sp|P35033|TRY3_SALSA   Trypsin III precursor
         Length = 238

 Score =  213 bits (542), Expect = 4e-54
 Identities = 98/227 (43%), Positives = 142/227 (62%), Gaps = 4/227 (1%)

Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            +E +K+V G  C K+S  +QA+L  SG+  CGG LI   WV++AAHC K  +QV LG+HN
Sbjct: 11  DEDDKIVGGYECRKNSASYQASLQ-SGYHFCGGSLISSTWVVSAAHCYKSRIQVRLGEHN 69

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +   E  ++ I   + I+HP YN    DNDIM++ L  P   +  +  + L + C+
Sbjct: 70  IAVNEGTEQFIDSVKVIMHPSYNSRNLDNDIMLIKLSKPASLNSYVSTVALPSSCASSGT 129

Query: 144 NCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C + GWG +   + ++PDT++C D+ ++     C  AYPG+IT +M CAG M+ G DSCQ
Sbjct: 130 RCLVSGWGNLSGSSSNYPDTLRCLDLPILSSSSCNSAYPGQITSNMFCAGFMEGGKDSCQ 189

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+VC G+L+G+VSWG    C   + KPGVYT VC +   WI + +
Sbjct: 190 GDSGGPVVCNGQLQGVVSWG-YGCAQRNKPGVYTKVCNYRSWISSTM 235
```

```
         GD+GGP+VC G L+G+VSWG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 185 GDAGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 230
```

>gi|14719441|pdb|1F7Z|A S Chain A, Rat Trypsinogen K15a Complexed With Bovine Panc:
Trypsin Inhibitor
Length = 233

```
 Score =  214 bits (544), Expect = 2e-54
 Identities = 99/227 (43%), Positives = 150/227 (66%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ + +V G  C ++S P+Q +L  SG+   CGG LI+ QWV++AAHC K   +QV LG+HN
Sbjct: 6    DDDDAIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHN 64

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +    E  ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+
Sbjct: 65   INVLEGNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGT 124

Query: 144 NCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQ
Sbjct: 125 QCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQ 184

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+VC G L+G+VSWG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 185 GDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 230
```

>gi|6755891|ref|NP_035775.1| G protease, serine, 3 [Mus musculus]
gi|2358088|gb|AAB69059.1| G trypsinogen 11 [Mus musculus]
Length = 246

```
 Score =  213 bits (543), Expect = 3e-54
 Identities = 105/242 (43%), Positives = 155/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+   CGG LI+ QWV++AA
Sbjct: 4    LLILALVGAAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+    E  ++ ++   + I HP +N +T +NDIM++ L +PV  + +
Sbjct: 63   HCYKTRIQVRLGEHNINVLEGNEQFVNAAKIIKHPNFNRKTLNNDIMLLKLSSPVTLNAR 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+      C I GWG  +      PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 123 VATVALPSSCAPAGTQCLISGWGNTLSFGVSEPDLLQCLDAPLLPQADCEASYPGKITGN 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVCAG ++ G DSCQGDSGGP+VC   L+G+VSWG    C    + PGVYT VC ++ WIQ+
Sbjct: 183 MVCAGFLEGGKDSCQGDSGGPVVCNRELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 241

Query: 247 IL 248
             +
Sbjct: 242 TI 243
```

```
          +   E  ++ ++  + I HP +N  T +NDIM++ L +PV  + ++  + L + C+
Sbjct: 96  INVLEGNEQFVNSAKIIKHPNFNSRTLNNDIMLIKLASPVTLNARVATVALPSSCAPAGT 155

Query: 144 NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG   +   + PD +QC D  L+P+  CE +YPGKIT +M+C G ++ G DSCQ
Sbjct: 156 QCLISGWGNTLSFGVNNPDLLQCLDAPLLPQADCEASYPGKITNNMICVGFLEGGKDSCQ 215

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+VC G+L+G+VSWG   C  K+ PGVYT VC ++ WIQ+ +
Sbjct: 216 GDSGGPVVCNGQLQGIVSWG-YGCALKDNPGVYTKVCNYVDWIQDTI 261
```

>gi|27573668|pdb|1J14|A Chain A, Benzamidine In Complex With Rat Trypsin Mutant X
gi|10120746|pdb|1QL9|A Chain A, Factor Xa Specific Inhibitor In Complex With Rat T
Mutant X99rt
Length = 223

```
 Score = 215 bits (548), Expect = 8e-55
 Identities = 100/222 (45%), Positives = 148/222 (66%), Gaps = 4/222 (1%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1   IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
             ++ ++  + I HP ++ ET++NDIM++ L +PVK + ++  + L + C+     C I
Sbjct: 60  GNEQFVNAAKIIKHPNFDRETYNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149 GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120 GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+VSWG   C   + PGVYT VC ++ WIQ+ +
Sbjct: 180 PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

>gi|4139560|pdb|3TGJ|E Chain E, S195a Trypsinogen Complexed With Bovine Pancreat:
Inhibitor (Bpti)
Length = 233

```
 Score = 215 bits (547), Expect = 1e-54
 Identities = 99/227 (43%), Positives = 151/227 (66%), Gaps = 4/227 (1%)

Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN
Sbjct: 6   DDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHN 64

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +   E  ++ ++  + I HP ++ +T +NDIM++ L +PVK + ++  + L + C+
Sbjct: 65  INVLEGNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGT 124

Query: 144 NCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQ
Sbjct: 125 QCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQ 184

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
```

```
Query: 61   PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
             QWV++AAHC K   +QV LG+HN+    E   ++ ++    + I HP ++ +T +NDIM++ L
Sbjct: 100  DQWVVSAAHCYKSRIQVRLGEHNINVLEGDEQFVNAAKIIKHPNFDRKTLNNDIMLIKLS 159

Query: 121  NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERA 178
            +PVK + ++   + L + C+      C I GWG    +    + PD +QC D   L+P+   CE +
Sbjct: 160  SPVKLNARVATVALPSSCAPAGTQCLISGWGNTLSFGVNDPDLLQCLDAPLLPQADCEAS 219

Query: 179  YPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVC 238
            YPGKIT +MVCAG ++ G DSCQGDSGGP+VC G L+G+VSWG    C    + PGVYT VC
Sbjct: 220  YPGKITNNMVCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVC 278

Query: 239  THIRWIQNIL 248
             ++ WIQ+ +
Sbjct: 279  NYVDWIQDTI 288
```

>gi|56541274|gb|AAH87610.1| Hypothetical LOC496627 [Xenopus tropicalis]
gi|58332100|ref|NP_001011202.1| hypothetical LOC496627 [Xenopus tropicalis]
Length = 243

Score = 216 bits (549), Expect = 6e-55
Identities = 100/243 (41%), Positives = 155/243 (63%), Gaps = 5/243 (2%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK+L +C++L   +A + + +K++ G  C ++S P+ +L  SG+  CGG LI  QWV++A
Sbjct: 1    MKLLLICVLLGAAA-AFDDDKIIGGSTCARNSVPYIVSL-NSGYHFCGGSLISNQWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K ++QV LG+HN+  +E  ++ I+  + I HP YN  T DNDIM++ L +P   +
Sbjct: 59   AHCYKASVQVRLGEHNIALSEGTEQFINSAKVIRHPSYNSRTIDNDIMLIKLASPASLNS 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLVPREQCERAYPGKITQ 185
             +  + L + C+    +C + GWG +     ++PD +QC +  ++   QC  AYPG+IT
Sbjct: 119  AVNTVALPSSCAAAGTSCLVSGWGNLSTTTSNYPDLLQCLNAPILTTAQCSGAYPGQITN 178

Query: 186  SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            +M CAG ++ G DSCQGDSGGP+VC G L+G+VSWG + C   +  PGVY  VC +  WIQ
Sbjct: 179  NMFCAGFLEGGKDSCQGDSGGPVVCNGELQGVVSWG-IGCAQRNYPGVYAKVCNYNSWIQ 237

Query: 246  NIL 248
             + +
Sbjct: 238  STI 240
```

>gi|51711962|ref|XP_487918.1| PREDICTED: similar to trypsinogen 9 [Mus musculus]
Length = 264

Score = 215 bits (548), Expect = 8e-55
Identities = 99/227 (43%), Positives = 149/227 (65%), Gaps = 4/227 (1%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN
Sbjct: 37   DDDDKIVGGYTCRENSIPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKTRIQVRLGEHN 95

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
```

```
 Score =  216 bits (550), Expect = 5e-55
 Identities = 100/227 (44%), Positives = 151/227 (66%), Gaps = 4/227 (1%)

Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN
Sbjct: 11  DDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHN 69

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +   E  ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+
Sbjct: 70  INVLEGNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGT 129

Query: 144 NCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQ
Sbjct: 130 QCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQ 189

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+VC G L+G+VSWG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 190 GDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 235


 >gi|34855584|ref|XP_342669.1|  G similar to trypsinogen 9 [Rattus norvegicus]
          Length = 246

 Score =  216 bits (550), Expect = 5e-55
 Identities = 103/242 (42%), Positives = 156/242 (64%), Gaps = 5/242 (2%)

Query: 10  MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV    A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4   LLFLALVGVAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ ++   + I HP +N    +NDIM++ L +PVK + +
Sbjct: 63  HCYKTRIQVRLGEHNINVLEGDEQFVNAAKIIKHPNFNARNLNNDIMLIKLSSPVKLNAR 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+     C I GWG  +    + PD +QC D  ++P+  CE +YPGKIT +
Sbjct: 123 VATVALPSSCAPAGTQCLISGWGNTLSLGVNNPDLLQCLDAPVLPQADCEASYPGKITNN 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M+C G ++ G DSCQGDSGGP+VC G+L+G+VSWG    C  K+ PGVYT VC ++ WIQ+
Sbjct: 183 MICVGFLEGGKDSCQGDSGGPVVCNGQLQGIVSWG-YGCALKDNPGVYTKVCNYVDWIQD 241

Query: 247 IL 248
             +
Sbjct: 242 TI 243


 >gi|34855588|ref|XP_342672.1|  G similar to trypsin (EC 3.4.21.4) II precursor - rat
            norvegicus]
           Length = 291

 Score =  216 bits (549), Expect = 6e-55
 Identities = 106/250 (42%), Positives = 159/250 (63%), Gaps = 5/250 (2%)

Query: 2   PMKMLTMKMLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID 60
            P + L   +L    LV  + A+  ++ +K+V G  C + S P+Q +L  SG+  CGG LI+
Sbjct: 41  PSRTLKDCLLNHLLVFIQVAFPVDDDDKIVGGYTCQEHSVPYQVSL-NSGYHYCGGSLIN 99
```

```
gi|47169490|tpe|CAE48382.1|  G TPA: trypsin 10 [Rattus norvegicus]
         Length = 246

 Score =  216 bits (551), Expect = 3e-55
 Identities = 106/242 (43%), Positives = 157/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAW-SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
             +L L LV A   A+ + + +K+V G  C ++S P+Q +L   SG+  CGG LI+ QWV++AA
Sbjct: 4    VLILALVGAAVAFPAADDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINEQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
             HC K   +QV LG+HN+    E   ++ ++   + I HP +   +T +NDIM++ L +PVK + +
Sbjct: 63   HCYKSRIQVRLGEHNINVLEGNEQFVNAAKIIKHPNFIRKTLNNDIMLIKLSSPVKLNSR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQS 186
             +   + L + C+      C I GWG     +      + PD +QC D  L+P+   CE +YPGKIT +
Sbjct: 123  VATVALPSSCAPAGTQCLISGWGNTLSFGVNEPDLLQCLDAPLLPQADCEASYPGKITDN 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
             MVCAG ++ G DSCQGDSGGP+VC G L+G+VSWG    C      + PGVYT VC ++ WIQ+
Sbjct: 183  MVCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 241

Query: 247  IL 248
              +
Sbjct: 242  TI 243


>gi|2358117|gb|AAB69087.1|   trypsinogen 15 [Mus musculus]
         Length = 246

 Score =  216 bits (551), Expect = 3e-55
 Identities = 106/241 (43%), Positives = 155/241 (64%), Gaps = 5/241 (2%)

Query: 11   LALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
             L L LV A  A+  ++ +K+V G  C ++S P+Q +L   SG+  CGG LI+ QWV++AAH
Sbjct: 5    LILALVGAAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAH 63

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
             C K   +QV LG+HN+    E   ++ ++   + I HP +N +T +NDIM++ L +PV   + ++
Sbjct: 64   CYKTRIQVRLGEHNINVLEGNEQFVNAAKIIKHPNFNRKTLNNDIMLIKLSSPVTLNARV 123

Query: 130  QPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQSM 187
               + L + C+      C I GWG     +      PD +QC D  L+P+   CE +YPGKIT +M
Sbjct: 124  ATVALPSSCAPAGTQCLISGWGNTLSFGVSEPDLLQCLDAPLLPQADCEASYPGKITGNM 183

Query: 188  VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
             VCAG ++ G DSCQGDSGGP+VC G L+G+VSWG    C      + PGVYT VC ++ WIQ+
Sbjct: 184  VCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDT 242

Query: 248  L 248
             +
Sbjct: 243  I 243


>gi|758266|emb|CAA24581.1|  G unnamed protein product [Rattus norvegicus]
         Length = 238
```

```
gi|2358118|gb|AAB69088.1|  G trypsinogen 16 [Mus musculus]
gi|3916748|gb|AAC79093.1|  G trypsinogen 16 [Mus musculus]
         Length = 246

 Score =  217 bits (552), Expect = 3e-55
 Identities = 107/242 (44%), Positives = 155/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4    LLFLALVGAAVAFPVDDDDKIVGGYTCRENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ I   + I HP +N +T +NDIM++ L +PV  + +
Sbjct: 63   HCYKTRIQVRLGEHNINVLEGNEQFIDAAKIIKHPNFNRKTLNNDIMLIKLSSPVTLNAR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+     C I GWG    +     PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 123  VATVALPSSCAPAGTQCLISGWGNTLSFGVSEPDLLQCLDAPLLPQADCEASYPGKITGN 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVCAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 183  MVCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 241

Query: 247  IL 248
             +
Sbjct: 242  TI 243


>gi|28373261|pdb|1CO7|E  S Chain E, R117h Mutant Rat Anionic Trypsin Complexed With
          Pancreatic Trypsin Inhibitor (Bpti)
         Length = 245

 Score =  217 bits (552), Expect = 3e-55
 Identities = 106/242 (43%), Positives = 158/242 (65%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAWS-EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L LV A  A+  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 3    LLFLALVGAAVAFPVDDDDKIVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAA 61

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+   E  ++ ++   + I HP ++ +T +NDIM++ L +PVK +
Sbjct: 62   HCYKSRIQVRLGEHNINVLEGNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNAH 121

Query: 129  IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L + C+     C I GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +
Sbjct: 122  VATVALPSSCAPAGTQCLISGWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDN 181

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVC G ++ G DSCQGDSGGP+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+
Sbjct: 182  MVCVGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQD 240

Query: 247  IL 248
             +
Sbjct: 241  TI 242


>gi|51871601|ref|NP_001004097.1|  G trypsin 10 precursor [Rattus norvegicus]
```

```
Query: 247 IL 248
            +
Sbjct: 242 TI 243
```

>gi|27545370|ref|NP_775423.1| preprotrypsinogen IV [Rattus norvegicus]
gi|56814|emb|CAA33718.1| preprotrypsinogen IV (AA -15 to 232) [Rattus norvegicus]
gi|92924|pir||S05494 trypsin (EC 3.4.21.4) IV precursor - rat
gi|136419|sp|P12788|TRY4_RAT Trypsin IV precursor (Pretrypsinogen IV)
Length = 247

Score = 210 bits (535), Expect = 2e-53
Identities = 95/228 (41%), Positives = 141/228 (61%), Gaps = 3/228 (1%)

```
Query: 25  EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNL 84
            + +K+V G  C K   P+Q +L+      CGG LI  QWVL+AAHC K  LQV LG+HN+
Sbjct: 20  DDDKIVGGYTCPKHLVPYQVSLHDGISHQCGGSLISDQWVLSAAHCYKRKLQVRLGEHNI 79

Query: 85  RQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPN 144
               E  ++ I  ++ I HP YN +T DNDIM++ LK+P   + ++  + L   C+    +
Sbjct: 80  HVLEGGEQFIDAEKIIRHPEYNKDTLDNDIMLIKLKSPAVLNSQVSTVSLPRSCASTDAQ 139

Query: 145 CQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQG 202
            C + GWG   +  G +P  +QC +  ++    C+++YPG+IT +M C G ++ G DSC G
Sbjct: 140 CLVSGWGNTVSIGGKYPALLQCLEAPVLSASSCKKSYPGQITSNMFCLGFLEGGKDSCDG 199

Query: 203 DSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            DSGGP+VC G ++G+VSWG + C  + KPGVYT VC ++ WIQ  + N
Sbjct: 200 DSGGPVVCNGEIQGIVSWGSV-CAMRGKPGVYTKVCNYLSWIQETMAN 246
```

>gi|67550|pir||TRPGTR trypsin (EC 3.4.21.4) precursor - pig (tentative sequence)
gi|136429|sp|P00761|TRYP_PIG Trypsin precursor
Length = 231

Score = 210 bits (535), Expect = 2e-53
Identities = 95/228 (41%), Positives = 141/228 (61%), Gaps = 4/228 (1%)

```
Query: 23  SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKH 82
            +++ +K+V G  C  +S P+Q +L +  H  CGG LI+ QWV++AAHC K  +QV LG+H
Sbjct: 3   TDDDDKIVGGYTCAANSIPYQVSLNSGSHF-CGGSLINSQWVVSAAHCYKSRIQVRLGEH 61

Query: 83  NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
            N+   E  ++ I+  + I HP +N  T DNDIM++ L +P   + ++  + L   C+
Sbjct: 62  NIDVLEGNEQFINAAKIITHPNFNGNTLDNDIMLIKLSSPATLNSRVATVSLPRSCAAAG 121

Query: 143 PNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
              C I GWG  K     +P  +QC    ++    C+ +YPG+IT +M+C G ++ G DSC
Sbjct: 122 TECLISGWGNTKSSGSSYPSLLQCLKAPVLSDSSCKSSYPGQITGNMICVGFLEGGKDSC 181

Query: 201 QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            QGDSGGP+VC G+L+G+VSWG   C  K KPGVYT VC ++ WIQ  +
Sbjct: 182 QGDSGGPVVCNGQLQGIVSWG-YGCAQKNKPGVYTKVCNYVNWIQQTI 228
```

```
>gi|67552|pir||TRDG   trypsin (EC 3.4.21.4) precursor, anionic - dog
 gi|136411|sp|P06872|TRY2_CANFA   Anionic trypsin precursor
 gi|164095|gb|AAA30899.1|   anionic trpysinogen precursor
          Length = 247

 Score =  210 bits (535), Expect = 2e-53
 Identities = 98/228 (42%), Positives = 149/228 (65%), Gaps = 4/228 (1%)

Query: 23   SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKH 82
             +++ +K+V G  C ++S P+Q +L  +G+  CGG LI  QWV++AAHC K  +QV LG++
Sbjct: 18   TDDDDKIVGGYTCEENSVPYQVSL-NAGYHFCGGSLISDQWVVSAAHCYKSRIQVRLGEY 76

Query: 83   NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
             N+   E  ++ I+  + I HP YN    DNDIM++ L +P   + ++  + L   C+
Sbjct: 77   NIDVLEGNEQFINSAKVIRHPNYNSWILDNDIMLIKLSSPAVLNARVATISLPRACAAPG 136

Query: 143  PNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
               C I GWG  + +G ++P+ +QC D  ++ + QCE +YPG+IT++M+CAG ++ G DSC
Sbjct: 137  TQCLISGWGNTLSSGTNYPELLQCLDAPILTQAQCEASYPGQITENMICAGFLEGGKDSC 196

Query: 201  QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             QGDSGGP+VC G L+G+VSWG   C  K KPGVYT VC  + WIQ+ +
Sbjct: 197  QGDSGGPVVCNGELQGIVSWG-YGCAQKNKPGVYTKVCNFVDWIQSTI 243


>gi|51714019|ref|XP_489834.1|  G  similar to Try10-like trypsinogen [Mus musculus]
 gi|51092303|ref|NP_001003664.1|  G  Try10-like trypsinogen [Mus musculus]
 gi|33186826|tpe|CAD68170.1|  G  TPA: Try10-like trypsinogen [Mus musculus]
          Length = 246

 Score =  210 bits (535), Expect = 2e-53
 Identities = 96/227 (42%), Positives = 147/227 (64%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +++V G  C ++S P+Q +L  SG+  CG  LI+ QWV++AAHC    +QV LG+HN
Sbjct: 19   DDDDRIVGGYTCRENSVPYQVSL-NSGYHFCGDSLINDQWVVSAAHCYNSRIQVRLGEHN 77

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +   E  ++ I     + HP++  +T DNDIM++ L +PV  + ++  + + + C+
Sbjct: 78   INVLEGNEQFIDAANIVKHPKFKKKTLDNDIMLIKLSSPVTLNARVATVAMPSSCALAGT 137

Query: 144  NCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +M+C G ++ G DSCQ
Sbjct: 138  QCLISGWGNTLSSGVNNPDLLQCLDAPLLPQADCEASYPGKITNNMICVGFLEGGKDSCQ 197

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDS GP+VC G+L+G+VSWG   C  K+ PGVYT VC ++ WIQN +
Sbjct: 198  GDSDGPVVCNGQLQGIVSWG-YGCAQKDNPGVYTKVCNYVDWIQNTI 243


>gi|6851258|gb|AAF29490.1|   tissue kallikrein [Saguinus oedipus]
          Length = 261

 Score =  210 bits (535), Expect = 2e-53
 Identities = 101/257 (39%), Positives = 155/257 (60%), Gaps = 16/257 (6%)
```

```
Query: 8    MKMLALCLVLA---KSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M  L LCL L+     A    Q ++V G   C + S P+QAALY       CGGVL+ PQWV
Sbjct: 1    MWFLVLCLALSLGGTGAVPPIQSRIVGGWDCKQHSQPWQAALYHYSTFQCGGVLVHPQWV 60

Query: 65   LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP-----------ETHDND 113
            LTAAHC    + Q+ LG+H+L + E    + + V ++  HP +N             E + +D
Sbjct: 61   LTAAHCISDHYQLWLGRHDLFENEDTAQFVFVSKSFPHPDFNMSLLKNHTRLPGEDYSHD 120

Query: 114  IMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWG--KMENGDFPDTIQCADVHLVP 171
            +M++ LK PV+ +   ++ + L   +  E    C    GWG  K E    FPD +QC D+ ++P
Sbjct: 121  LMLLQLKQPVQITDAVKVVELPTEGIEVGSTCLASGWGSIKPEKFSFPDILQCVDLKILP 180

Query: 172  REQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKP 231
             ++C++A++  K+T+ M+CAG +K+G D+C GDSGGPL C G L+G++SWG +PCGS  KP
Sbjct: 181  NDECDKAHAQKVTEFMLCAGPLKDGQDTCVGDSGGPLTCDGVLQGIISWGYIPCGSPNKP 240

Query: 232  GVYTDVCTHIRWIQNIL 248
             V+   V ++++WI++ +
Sbjct: 241  SVFVRVLSYVKWIKDTI 257
```

>gi|34810822|pdb|1OPH|B Chain B, Non-Covalent Complex Between Alpha-1-Pi-Pittsbu
S195a Trypsin
Length = 243

Score = 210 bits (535), Expect = 2e-53
Identities = 96/227 (42%), Positives = 143/227 (62%), Gaps = 4/227 (1%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G   C   ++ P+Q +L   SG+   CGG LI+ QWV++AAHC K   +QV LG+ N
Sbjct: 16   DDDDKIVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDN 74

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +    E  ++ IS   ++IVHP YN   T +NDIM++ LK+      + ++   + L    C+
Sbjct: 75   INVVEGNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGT 134

Query: 144  NCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG  K      +PD ++C      ++     C+ AYPG+IT +M CAG ++ G DSCQ
Sbjct: 135  QCLISGWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQ 194

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GD+GGP+VC G+L+G+VSWG     C  K KPGVYT VC ++  WI+  +
Sbjct: 195  GDAGGPVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 240
```

>gi|2098545|pdb|1ANC| Anionic Trypsin Mutant With Ser 214 Replaced By Lys
Length = 223

Score = 210 bits (535), Expect = 2e-53
Identities = 98/222 (44%), Positives = 146/222 (65%), Gaps = 4/222 (1%)

```
Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G   C ++S P+Q +L   SG+   CGG LI+ QWV++AAHC K  +QV LG+HN+    E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+      C I
```

```
Sbjct: 60   GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149 GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120 GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+V WG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 180 PVVCNGELQGIVKWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

>gi|2098541|pdb|1ANB| Anionic Trypsin Mutant With Ser 214 Replaced By Glu
Length = 223

Score = 210 bits (535), Expect = 2e-53
Identities = 98/222 (44%), Positives = 146/222 (65%), Gaps = 4/222 (1%)

```
Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
               ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+      C I
Sbjct: 60   GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149 GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120 GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+V WG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 180 PVVCNGELQGIVEWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

>gi|11513886|pdb|1FY8|E Chain E, Crystal Structure Of The Deltaile16val17 Rat An
Trypsinogen-Bpti Complex
Length = 231

Score = 210 bits (534), Expect = 3e-53
Identities = 98/219 (44%), Positives = 145/219 (66%), Gaps = 4/219 (1%)

```
Query: 32   GGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQ 91
             G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E  +
Sbjct: 12   GYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLEGNE 70

Query: 92   RQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWG 151
             + ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+      C I GWG
Sbjct: 71   QFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLISGWG 130

Query: 152 K-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLV 209
              + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGGP+V
Sbjct: 131 NTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGGPVV 190

Query: 210 CGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            C G L+G+VSWG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 191 CNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 228
```

```
>gi|9257000|pdb|1EZU|D  Chain D, Ecotin Y69f, D70p Bound To D102n Trypsin
 gi|9256999|pdb|1EZU|C  Chain C, Ecotin Y69f, D70p Bound To D102n Trypsin
 gi|9256996|pdb|1EZS|D  Chain D, Crystal Structure Of Ecotin Mutant M84r, W67a, G68a
          D70a Bound To Rat Anionic Trypsin Ii
 gi|9256995|pdb|1EZS|C  Chain C, Crystal Structure Of Ecotin Mutant M84r, W67a, G68a
          D70a Bound To Rat Anionic Trypsin Ii
         Length = 223

 Score =  210 bits (534), Expect = 3e-53
 Identities = 98/222 (44%), Positives = 147/222 (66%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
               ++ ++   + I HP ++ +T +N+IM++ L +PVK + ++   + L + C+     C I
Sbjct: 60   GDEQFVNAAKIIKHPNFDRKTLNNNIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149  GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
             GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120  GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             P+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 180  PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220


>gi|2392288|pdb|1DPO|  Structure Of Rat Trypsin
         Length = 223

 Score =  210 bits (534), Expect = 3e-53
 Identities = 98/222 (44%), Positives = 146/222 (65%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
               ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+     C I
Sbjct: 60   GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149  GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
             GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGD GG
Sbjct: 120  GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDCGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             P+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 180  PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220


>gi|230776|pdb|2TRM|  Asn102Trypsin (E.C.3.4.21.4) (Mutant With Asp 102 Replaced
          (D102N) Complex With Benzamidine At pH 8 (Anionic
          Isozyme)
```

gi|230384|pdb|1TRM|B S Chain B, Asn102Trypsin (E.C.3.4.21.4) (Mutant With Asp 102 Re
By Asn) (D102N) Complex With Benzamidine At pH 6
(Anionic Isozyme)
gi|230383|pdb|1TRM|A S Chain A, Asn102Trypsin (E.C.3.4.21.4) (Mutant With Asp 102 Re
By Asn) (D102N) Complex With Benzamidine At pH 6
(Anionic Isozyme)
Length = 223

```
 Score =  210 bits (534), Expect = 3e-53
 Identities = 98/222 (44%), Positives = 147/222 (66%), Gaps = 4/222 (1%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C ++S P+Q +L   SG+  CGG LI+ QWV++AAHC K   +QV LG+HN+    E
Sbjct: 1   IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ ++   + I HP ++ +T +N+IM++ L +PVK + ++  + L + C+      C I
Sbjct: 60  GNEQFVNAAKIIKHPNFDRKTLNNNIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149 GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G DSCQGDSGG
Sbjct: 120 GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 180 PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220
```

>gi|56541161|gb|AAH87563.1| G Unknown (protein for MGC:97681) [Xenopus tropicalis]
gi|58332102|ref|NP_001011199.1| G hypothetical LOC496623 [Xenopus tropicalis]
Length = 243

```
 Score =  209 bits (533), Expect = 4e-53
 Identities = 101/243 (41%), Positives = 151/243 (62%), Gaps = 5/243 (2%)

Query: 8   MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            MK+  LC++L  +A + + +K++ G  C K+S P+  +L  SG+  CGG LI+ QWV++A
Sbjct: 1   MKLFLLCVLLGAAA-AFDDDKIIGGATCAKNSVPYIVSL-NSGYHFCGGSLINNQWVVSA 58

Query: 68  AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K ++QV LG+HN+  +E  ++ IS  + I H  YN  T DNDIM++ L +    +
Sbjct: 59  AHCYKASIQVRLGEHNIALSEGTEQFISSSKVIRHSGYNSWTLDNDIMLIKLSSAASLNA 118

Query: 128 KIQPLPLKNDCSEENPNCQILGWGK--MENGDFPDTIQCADVHLVPREQCERAYPGKITQ 185
             +  + L + C+    +C I GWG       ++PD +QC    ++    QC  AYPG+IT
Sbjct: 119 AVNAVALPSGCAAAGASCLISGWGNTLSSGSNYPDLLQCLYAPILTDAQCNNAYPGEITN 178

Query: 186 SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            +M+C G ++ G DSCQGDSGGP+VC G L+G+VSWG   C  +  PGVYT VC +  WIQ
Sbjct: 179 NMICLGFLEGGKDSCQGDSGGPVVCNGELQGVVSWG-YGCAQRNYPGVYTKVCNYNSWIQ 237

Query: 246 NIL 248
            + +
Sbjct: 238 STI 240
```

```
>gi|2781042|pdb|1AMH|B  Chain B, Uncomplexed Rat Trypsin Mutant With Asp 189 Repla
          Ser (D189s)
 gi|2781041|pdb|1AMH|A  Chain A, Uncomplexed Rat Trypsin Mutant With Asp 189 Replace
          Ser (D189s)
         Length = 223

 Score =  209 bits (533), Expect = 4e-53
 Identities = 98/222 (44%), Positives = 146/222 (65%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ ++  + I HP ++ +T +NDIM++ L +PVK + ++  + L + C+     C I
Sbjct: 60   GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149  GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G  SCQGDSGG
Sbjct: 120  GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKSSCQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 180  PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220


>gi|55649807|ref|XP_524358.1|  PREDICTED: similar to variant form hippostasin/KLK:
          troglodytes]
         Length = 533

 Score =  209 bits (532), Expect = 6e-53
 Identities = 104/274 (37%), Positives = 153/274 (55%), Gaps = 31/274 (11%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M++L L L+   +     + +++ G  C   S P+QAAL+    LLCG  LI P+W+LTA
Sbjct: 259  MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTA 318

Query: 68   AHCKKPNLQ-------------------------VILGKHNLRQTETFQRQISVDRTIVH 102
            AHC+KP +                          V LG+HNL++ E  ++  +   +  H
Sbjct: 319  AHCRKPWVSLTSPTHVSPDLSSSNYCLSHLSRYIVHLGQHNLQKEEGCEQTQTATESFPH 378

Query: 103  PRYNP----ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF 158
            P +N     + H NDIM+V + +PV  +  ++PL L + C     +C I GWG   +
Sbjct: 379  PGFNDSLPNKDHRNDIMLVKMASPVSITWAVRPLTLSSRCVTAGTSCLISGWGSTSSPQL 438

Query: 159  --PDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRG 216
              P T++CA++ ++  ++CE AYPG IT +MVCA   + G DSCQGDSGGPLVC   L+G
Sbjct: 439  RLPHTLRCANITIIEHQKCENAYPGNITDTMVCASVREGGKDSCQGDSGGPLVCNESLQG 498

Query: 217  LVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            ++SWG  PC    KPGVYT VC ++ WIQ  ++N
Sbjct: 499  IISWGQDPCAITRKPGVYTKVCKYVDWIQETMKN 532


 Score =  129 bits (325), Expect = 6e-29
 Identities = 75/231 (32%), Positives = 117/231 (50%), Gaps = 40/231 (17%)
```

```
Query: 6   LTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVL 65
           L++ +L   L L+++A      K+ +G  C ++S P+Q  L+    L CGGVLID +WVL
Sbjct: 3   LSIFLLLCVLGLSQAA----TPKIFNGTECGRNSQPWQVGLFEGTSLRCGGVLIDHRWVL 58

Query: 66  TAAHCKKPNLQ-------------------------------VILGKHNLRQTETFQRQI 94
           TAAHC     +                               V LG+H+L Q +  ++
Sbjct: 59  TAAHCSGSGERQERLGVSVEGCKVDGCVPATRSAVATGSRYWVRLGEHSLSQLDWTEQIR 118

Query: 95  SVDRTIVHPRY--NPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGK 152
               ++ HP Y     +H++D+ ++ L+ PV+ +  +QPLPL NDC+     C + GWG
Sbjct: 119 RSGFSVTHPGYLGASTSHEHDLRLLRLRLPVRVTSSVQPLPLPNDCATAGTECHVSGWGI 178

Query: 153 MEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
            +     FPD +QC ++ +V    C   YPG+IT +MVCAG +  G D+CQ
Sbjct: 179 TNHPWNPFPDLLQCLNLSIVSHATCHDVYPGRITSNMVCAGGV-PGQDACQ 228
```

>gi|58257847|gb|AAW69366.1| try14 [Macaca mulatta]
Length = 247

Score = 209 bits (532), Expect = 6e-53
Identities = 98/227 (43%), Positives = 146/227 (64%), Gaps = 4/227 (1%)

```
Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
           ++ +K+V G  C ++S P+Q +L +  H  CGG LI+ QWV++AAHC KP +QV LG+HN
Sbjct: 19  DDDDKIVGGYTCEENSLPYQVSLNSGSHF-CGGSLINKQWVVSAAHCYKPRIQVRLGEHN 77

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
           ++  E  ++ I   + I HP+YN ET DNDIM+V L  P   + ++  + L +  +
Sbjct: 78  IKVLEGNEQFIHAAKIIRHPKYNNETLDNDIMLVKLSTPAIINARVSTISLPSALAAAGT 137

Query: 144 NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
            C I GWG   +   D+PD +QC D  ++ + +CE +YPGKIT +M C G ++ G DSCQ
Sbjct: 138 ECLISGWGNTLSFGADYPDELQCLDAPVLTQAKCEASYPGKITSNMFCVGFLEGGKDSCQ 197

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            DSGGP+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 198 RDSGGPVVCNGQLQGVVSWG-YGCARKNRPGVYTKVYNYVDWIRDTI 243
```

>gi|50979094|ref|NP_001003284.1| G kallikrein 2, prostatic [Canis familiaris]
gi|868|emb|CAA68720.1| G precursor [Canis familiaris]
gi|119586|sp|P09582|ESTA_CANFA G Arginine esterase precursor
Length = 260

Score = 209 bits (531), Expect = 7e-53
Identities = 97/257 (37%), Positives = 150/257 (58%), Gaps = 15/257 (5%)

```
Query: 8   MKMLALCLVLAKSAWSEE---QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
           M  LALCL ++      E   Q +++ G  CLK+S P+Q A+Y +G   CGGVL++P+WV
Sbjct: 1   MWFLALCLAMSLGWTGAEPHFQPRIIGGRECLKNSQPWQVAVYHNGEFACGGVLVNPEWV 60

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----------ETHDNDI 114
           LTAAHC   N +V LG+HNL ++E   + + V ++ +HP Y            E   +D+
Sbjct: 61  LTAAHCANSNCEVWLGRHNLSESEDEGQLVQVRKSFIHPLYKTKVPRAVIRPGEDRSHDL 120

Query: 115 MMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPR 172
```

```
           M++HL+ P K +K ++ + L           C + GWG  +     P ++QC D+ L+
Sbjct: 121 MLLHLEEPAKITKAVRVMDLPKKEPPLGSTCYVSGWGSTDPETIFHPGSLQCVDLKLLSN 180

Query: 173 EQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPG 232
             QC + Y  K+T+ M+CAG ++  D+C+GDSGGPL+C G L G+ SWG  PCG  + P
Sbjct: 181 NQCAKVYTQKVTKFMLCAGVLEGKKDTCKGDSGGPLICDGELVGITSWGATPCGKPQMPS 240

Query: 233 VYTDVCTHIRWIQNILR 249
           +YT V  H+ WI++ ++
Sbjct: 241 LYTRVMPHLMWIKDTMK 257
```

>gi|45382397|ref|NP_990715.1| G trypsinogen [Gallus gallus]
gi|1085254|pir||S55066 trypsin (EC 3.4.21.4) II precursor, pancreatic (clone 2-P29) chicken
gi|2499864|sp|Q90629|TRY3_CHICK G Trypsin II-P29 precursor
gi|603907|gb|AAA79914.1| G trypsinogen
Length = 248

Score = 209 bits (531), Expect = 7e-53
Identities = 105/248 (42%), Positives = 158/248 (63%), Gaps = 5/248 (2%)

```
Query: 3   MKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQ 62
            MK L + +  L   +A    +++ +K+V G  C + S P+Q +L  SG+  CGG LI+ Q
Sbjct: 1   MKFLFLILSCLGAAVAFPGGADD-DKIVGGYTCPEHSVPYQVSL-NSGYHFCGGSLINSQ 58

Query: 63  WVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNP 122
            WVL+AAHC K  +QV LG++N+   E  +  S    I HP+Y+  T +NDIM++ L +
Sbjct: 59  WVLSAAHCYKSRIQVRLGEYNIDVQEDSEVVRSSSVIIRHPKYSSITLNNDIMLIKLASA 118

Query: 123 VKFSKKIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYP 180
            V++S  IQP+ L + C++    C I GWG  + NG ++P+ +QC +  ++  ++C+ AYP
Sbjct: 119 VEYSADIQPIALPSSCAKAGTECLISGWGNTLSNGYNYPELLQCLNAPILSDQECQEAYP 178

Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
            G IT +M+C G ++ G DSCQGDSGGP+VC G L+G+VSWG + C  K  PGVYT VC +
Sbjct: 179 GDITSNMICVGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-IGCALKGYPGVYTKVCNY 237

Query: 241 IRWIQNIL 248
            + WIQ  +
Sbjct: 238 VDWIQETI 245
```

>gi|56971223|gb|AAH88079.1| G Hypothetical LOC496920 [Xenopus tropicalis]
gi|58332720|ref|NP_001011435.1| G hypothetical LOC496920 [Xenopus tropicalis]
Length = 251

Score = 209 bits (531), Expect = 7e-53
Identities = 97/250 (38%), Positives = 150/250 (60%), Gaps = 4/250 (1%)

```
Query: 5   MLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M+    + + L +A +A  ++ +K+V G  C   S P+Q      +G   CGG LI P+W+
Sbjct: 1   MMMPLWVLMFLAVAAAAPLDDDDKIVGGYECTPHSQPWQVLFTFNGRNWCGGSLISPRWI 60

Query: 65  LTAAHCKKP--NLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNP 122
            ++AAHC +P   L  +LG+H+L++ E ++ I V+    H Y E +D+DIM+V L  P
```

```
Sbjct: 61   ISAAHCYQPPKTLVALLGEHDLKKKEGTEQHIQVEAAYKHFGYKDEAYDHDIMLVKLAKP 120

Query: 123 VKFSKKIQPLPLKNDCSEENPNCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYP 180
             ++++ +QP+P+    C   +    C + G+G +    N   +PD +QC DV +V      C+ +YP
Sbjct: 121 AQYNQYVQPIPVARSCPTDGAKCLVSGYGNVLGYNTRYPDQLQCLDVPIVSDSSCKASYP 180

Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
              I+++M CAG ++ G   SC+GDSGGPL+C G L G VSWG   C SK  PGVY  VC +
Sbjct: 181 RMISENMFCAGFLEGGKGSCKGDSGGPLICNGELYGAVSWGGSYCISKNSPGVYAKVCNY 240

Query: 241 IRWIQNILRN 250
            + WI+NI  N
Sbjct: 241 LDWIKNITEN 250
```

>gi|25814806|gb|AAN75630.1| G trypsinogen [Gallus gallus]
Length = 248

Score = 208 bits (530), Expect = 9e-53
Identities = 100/226 (44%), Positives = 148/226 (65%), Gaps = 4/226 (1%)

```
Query: 25   EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNL 84
            + +K+V G  C + S P+Q +L  SG+  CGG LI+ QWVL+AAHC K  +QV LG++N+
Sbjct: 22   DDDKIVGGYTCPEHSVPYQVSL-NSGYHFCGGSLINSQWVLSAAHCYKSRIQVRLGEYNI 80

Query: 85   RQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPN 144
              E  +    S     I HP+Y+  T +NDIM++ L + V++S  IQP+ L + C++
Sbjct: 81   DVQEDSEVVRSSSVIIRHPKYSSITLNNDIMLIKLASAVEYSADIQPIALPSSCAKAGTE 140

Query: 145 CQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQG 202
            C I GWG  + NG ++P+ +QC +  ++  ++C+ AYPG IT +M+C G ++ G DSCQG
Sbjct: 141 CLISGWGNTLSNGYNYPELLQCLNAPILSDQECQEAYPGDITSNMICVGFLEGGKDSCQG 200

Query: 203 DSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            DSGGP+VC G L+G+VSWG + C  K  PGVYT VC ++ WIQ  +
Sbjct: 201 DSGGPVVCNGELQGIVSWG-IGCALKGYPGVYTKVCNYVDWIQETI 245
```

>gi|14719439|pdb|1F5R|A S Chain A, Rat Trypsinogen Mutant Complexed With Bovine Par
Trypsin Inhibitor
Length = 231

Score = 208 bits (530), Expect = 9e-53
Identities = 97/219 (44%), Positives = 145/219 (66%), Gaps = 4/219 (1%)

```
Query: 32   GGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQ 91
            G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+    E  +
Sbjct: 12   GYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLEGNE 70

Query: 92   RQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWG 151
            + ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+      C I GWG
Sbjct: 71   QFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLISGWG 130

Query: 152 K-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLV 209
              + +G + PD ++C D  L+P+   CE +YPGKIT +MVC G ++ G DSCQGDSGGP+V
Sbjct: 131 NTLSSGVNEPDLLKCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGDSGGPVV 190
```

```
Query: 210 CGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           C G L+G+VSWG    C    + PGVYT VC ++ WIQ+ +
Sbjct: 191 CNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 228
```

```
>gi|108957|pir||S13813  trypsin (EC 3.4.21.4) - bovine
 gi|2499861|sp|Q29463|TRY2_BOVIN  Anionic trypsin precursor
 gi|830|emb|CAA38513.1|  trypsinogen anionic precursor [Bos taurus]
          Length = 247

 Score =  208 bits (529), Expect = 1e-52
 Identities = 102/242 (42%), Positives = 155/242 (64%), Gaps = 5/242 (2%)

Query: 10   MLALCLVLAKSAW-SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L  V A  A+ S++ +K+V G  C ++S P+Q +L  +G+  CGG LI+ QWV++AA
Sbjct: 4    LLILAFVGAAVAFPSDDDDKIVGGYTCAENSVPYQVSL-NAGYHFCGGSLINDQWVVSAA 62

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC + ++QV LG++N+    E  ++ I    + I HP+Y+  T DNDI+++ L  P    + +
Sbjct: 63   HCYQYHIQVRLGEYNIDVLEGGEQFIDASKIIRHPKYSSWTLDNDILLIKLSTPAVINAR 122

Query: 129  IQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  L L + C+      C I GWG  + +G ++PD +QC    L+    CE +YPG+IT +
Sbjct: 123  VSTLLLPSACASAGTECLISGWGNTLSSGVNYPDLLQCLVAPLLSHADCEASYPGQITNN 182

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M+CAG ++ G DSCQGDSGGP+ C G+L+G+VSWG   C  K KPGVYT VC ++ WIQ
Sbjct: 183  MICAGFLEGGKDSCQGDSGGPVACNGQLQGIVSWG-YGCAQKGKPGVYTKVCNYVDWIQE 241

Query: 247  IL 248
             +
Sbjct: 242  TI 243
```

```
>gi|108118|pir||A37938  tissue kallikrein (EC 3.4.21.35), prostatic, precursor - do
 gi|163907|gb|AAA30831.1|  arginine esterase
          Length = 260

 Score =  208 bits (529), Expect = 1e-52
 Identities = 97/257 (37%), Positives = 149/257 (57%), Gaps = 15/257 (5%)

Query: 8    MKMLALCLVLAKSAWSEE---QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M  LALCL ++       E   Q +++ G  CLK+S P+Q A+Y +G   CGGVL+ P+WV
Sbjct: 1    MWFLALCLAMSLGWTGAEPHFQPRIIGGRECLKNSQPWQVAVYHNGEFACGGVLVHPEWV 60

Query: 65   LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----------ETHDNDI 114
            LTAAHC   N +V LG+HNL ++E   + + V ++ +HP Y            E   +D+
Sbjct: 61   LTAAHCANSNCEVWLGRHNLSESEDEGQLVQVRKSFIHPLYKTKVPRAVIRPGEDRSHDL 120

Query: 115  MMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPR 172
            M++HL+ P K +K ++ + L             C + GWG  +      P ++QC D+ L+
Sbjct: 121  MLLHLEEPAKITKAVRVMDLPKKEPPLGSTCYVSGWGSTDPETIFHPGSLQCVDLKLLSN 180

Query: 173  EQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPG 232
             QC + Y  K+T+ M+CAG ++    D+C+GDSGGPL+C G L G+ SWG  PCG  + P
Sbjct: 181  NQCAKVYTQKVTKFMLCAGVLEGKKDTCKGDSGGPLICDGELVGITSWGATPCGKPQMPS 240
```

```
Query: 233 VYTDVCTHIRWIQNILR 249
           +YT V  H+ WI++ ++
Sbjct: 241 LYTRVMPHLMWIKDTMK 257
```

>gi|2358072|gb|AAB69044.1| trypsinogen 7 [Mus musculus]
gi|38511906|gb|AAH61093.1| RIKEN cDNA 2210010C04 [Mus musculus]
gi|12842654|dbj|BAB25680.1| unnamed protein product [Mus musculus]
gi|12841533|dbj|BAB25246.1| unnamed protein product [Mus musculus]
Length = 247

Score = 208 bits (529), Expect = 1e-52
Identities = 99/246 (40%), Positives = 147/246 (59%), Gaps = 4/246 (1%)

```
Query: 5    MLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M T+   LA               ++ +K+V G  C +++ P+Q +L  SG+   CGG LI+ QWV
Sbjct: 1    MKTLIFLAFLGAAVALPLDDDDDKIVGGYTCQRNALPYQVSL-NSGYHFCGGSLINSQWV 59

Query: 65   LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
            ++AAHC K   +QV LG+HN+    E   ++ I    + I HP YN   T++NDIM++ LK
Sbjct: 60   VSAAHCYKSRIQVRLGEHNIDALEGGEQFIDAAKIIRHPNYNANTYNNDIMLIKLKTAAT 119

Query: 125  FSKKIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGK 182
             + ++  + L   C       C + GWG  + +G ++P  +QC D  ++    C  +YPGK
Sbjct: 120  LNSRVSTVALPRSCPSAGTRCLVSGWGNTLSSGTNYPSLLQCLDAPVLSDSSCTSSYPGK 179

Query: 183  ITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
            IT +M C G ++ G DSCQGDSGGP+VC G+L+G+VSWG   C   + KPGVYT VC ++
Sbjct: 180  ITSNMFCLGFLEGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRGKPGVYTKVCKYVN 238

Query: 243  WIQNIL 248
            WIQ  +
Sbjct: 239  WIQQTI 244
```

>gi|56556311|gb|AAH87753.1| LOC496635 protein [Xenopus tropicalis]
Length = 252

Score = 208 bits (529), Expect = 1e-52
Identities = 96/245 (39%), Positives = 146/245 (59%), Gaps = 3/245 (1%)

```
Query: 10   MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            +L + L+L  +A ++    +++ G  C+  S P+Q ALY     +CGGVLI+  WVLTAAH
Sbjct: 1    LLLVLLLLGSAAQTQTFHRIIGGEECVPHSQPWQVALYYFSDFICGGVLINEWWVLTAAH 60

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C + NLQV+LG HN  +     ++      +    H   ++P T+D+DIM++ L +     + ++
Sbjct: 61   CNQSNLQVLLGAHNRTKPTGHKQYTYAAKICPHCGFHPITYDHDIMLLKLASEADINTRV 120

Query: 130  QPLPLKNDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGK-ITQS 186
             P+PL +    +N  C   GWG    +    +PD +QC +V  V     C+  YP   IT +
Sbjct: 121  APIPLASYLVADNTECLASGWGSTTSPQETYPDNLQCVNVTTVSNSDCQACYPSDIITDN 180

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M+CAG+M   G D+C GDSGGPLVC G L G+ SWGD  CGS  KPG++  V  ++ WI +
Sbjct: 181  MLCAGNMAGGKDTCVGDSGGPLVCNGELHGITSWGDYVCGSPNKPGIFAKVFNYLNWISD 240
```

```
Query: 247 ILRNK 251
           I++N+
Sbjct: 241 IMQNE 245
```

>gi|14719487|pdb|3TGK|E Chain E, Trypsinogen Mutant D194n And Deletion Of Ile 16 Complexed With Bovine Pancreatic Trypsin Inhibitor (Bpti)
Length = 231

```
 Score =  208 bits (529), Expect = 1e-52
 Identities = 97/219 (44%), Positives = 145/219 (66%), Gaps = 4/219 (1%)

Query: 32   GGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQ 91
            G  C ++S P+Q +L  SG+   CGG LI+ QWV++AAHC K  +QV LG+HN+    E  +
Sbjct: 12   GYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLEGNE 70

Query: 92   RQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWG 151
            + ++   + I HP ++ +T +NDIM++ L +PVK + ++   + L + C+      C I GWG
Sbjct: 71   QFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLISGWG 130

Query: 152  K-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLV 209
              + +G + PD +QC D  L+P+   CE +YPGKIT +MVC G ++ G DSCQG+SGGP+V
Sbjct: 131  NTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKDSCQGNSGGPVV 190

Query: 210  CGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            C G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 191  CNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 228
```

>gi|57415|emb|CAA41752.1| trypsin V b-form [Rattus rattus]
gi|92927|pir||JQ1472 trypsin (EC 3.4.21.4) V precursor, b-form - rat
gi|418137|sp|P32822|TRYB_RAT Trypsin V-B precursor
Length = 246

```
 Score =  207 bits (528), Expect = 2e-52
 Identities = 97/223 (43%), Positives = 139/223 (62%), Gaps = 3/223 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            +   +++V G   C + S P+Q +L     H+ CGG LI   QWVL+AAHC   P LQV LG+HN
Sbjct: 20   DNDDRIVGGYTCQEHSVPYQVSLNAGSHI-CGGSLITDQWVLSAAHCYHPQLQVRLGEHN 78

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            + + E  ++ I   + I+HP Y+  T DNDIM++ LK+P   + K+  +PL   C
Sbjct: 79   IYEIEGAEQFIDAAKMILHPDYDKWTVDNDIMLIKLKSPATLNSKVSTIPLPQYCPTAGT 138

Query: 144  NCQILGWGKMENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQG 202
              C + GWG ++ G + P  +QC D ++   C +AYP +IT +M C G ++ G DSCQ
Sbjct: 139  ECLVSGWGVLKFGFESPSVLQCLDAPVLSDSVCHKAYPRQITNNMFCLGFLEGGKDSCQY 198

Query: 203  DSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            DSGGP+VC G ++G+VSWGD  C   + KPGVYT VC ++ WIQ
Sbjct: 199  DSGGPVVCNGEVQGIVSWGD-GCALEGKPGVYTKVCNYLNWIQ 240
```

>gi|27530958|dbj|BAC54105.1| variant form hippostasin/KLK11 [Homo sapiens]
Length = 275

Score = 207 bits (528), Expect = 2e-52
Identities = 104/274 (37%), Positives = 152/274 (55%), Gaps = 31/274 (11%)

```
Query: 8   MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M++L L L+   +     + +++ G  C   S P+QAAL+    LLCG  LI P+W+LTA
Sbjct: 1   MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTA 60

Query: 68  AHCKKPNLQ-------------------------VILGKHNLRQTETFQRQISVDRTIVH 102
            AHC KP +                          V LG+HNL++ E  ++  +   +  H
Sbjct: 61  AHCLKPWVSLTSPTHVSPDLSSSNYCLSHLSRYIVHLGQHNLQKEEGCEQTRTATESFPH 120

Query: 103 PRYNP----ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF 158
            P +N     + H NDIM+V + +PV  +  ++PL L + C     +C I GWG   +
Sbjct: 121 PGFNNSLPNKDHRNDIMLVKMASPVSITWAVRPLTLSSRCVTAGTSCLISGWGSTSSPQL 180

Query: 159 --PDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRG 216
              P T++CA++ ++  ++CE AYPG IT +MVCA   + G DSCQGDSGGPLVC   L+G
Sbjct: 181 RLPHTLRCANITIIEHQKCENAYPGNITDTMVCASVQEGGKDSCQGDSGGPLVCNQSLQG 240

Query: 217 LVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            ++SWG  PC    KPGVYT VC ++ WIQ  ++N
Sbjct: 241 IISWGQDPCAITRKPGVYTKVCKYVDWIQETMKN 274
```

>gi|47220857|emb|CAG00064.1| unnamed protein product [Tetraodon nigroviridis]
Length = 246

Score = 207 bits (528), Expect = 2e-52
Identities = 101/241 (41%), Positives = 147/241 (60%), Gaps = 7/241 (2%)

```
Query: 13  LCLVLAKSAWS---EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            + LVL  +A++   +E +K+V G  C K+S P+Q +L  SG+  CGG LI   WV++AAH
Sbjct: 5   IVLVLIAAAYAAPIDEDDKIVGGYECRKNSVPYQVSL-NSGYHFCGGSLISSSWVVSAAH 63

Query: 70  CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C K  +QV LG+HN+   E  ++ I   + I HPRYN    DNDIM++ L +P +    +
Sbjct: 64  CYKSRIQVRLGEHNIAVHEGTEQFIDSAKVITHPRYNSYNLDNDIMLIKLSSPARLDSYV 123

Query: 130 QPLPLKNDCSEENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSM 187
            + + L + C+     C I GWG   +   +FPD + C D  ++    C  +YPG IT +M
Sbjct: 124 RTVSLPSSCAGAGTYCLISGWGNTSSSGVNFPDNLMCLDAPILSDTSCRNSYPGGITANM 183

Query: 188 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
             CAG ++ G DSCQ DSGGP+VC G+L+G+VSWG+  C  K KPGVY  VC +  WI++
Sbjct: 184 FCAGFLEGGKDSCQVDSGGPVVCNGQLQGVVSWGE-GCAQKNKPGVYAKVCNYNSWIRDT 242

Query: 248 L 248
            +
Sbjct: 243 M 243
```

>gi|47220856|emb|CAG00063.1| unnamed protein product [Tetraodon nigroviridis]
Length = 278

```
 Score =  207 bits (528), Expect = 2e-52
 Identities = 101/247 (40%), Positives = 153/247 (61%), Gaps = 8/247 (3%)

Query: 7    TMKMLALCLVLAKSAWS---EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQW 63
            TMK    + LVL   +A++     +E +K+V G   C K+S P+Q +L   SG+   CGG LI     W
Sbjct: 34   TMKAF-IVLVLIAAAYAAPIDEDDKIVGGYECRKNSVPYQVSL-NSGYHFCGGSLISSSW 91

Query: 64   VLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPV 123
            V++AAHC K   +QV LG+HN+    E   ++ I+   + I HPRYN    DNDIM++ L +P
Sbjct: 92   VVSAAHCYKSRIQVRLGEHNIAVNEGTEQFINSAKVITHPRYNSYNLDNDIMLIKLSSPA 151

Query: 124  KFSKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPG 181
            +       + + L + C+     +C I GWG    +   ++PD + C +   ++     C   +YPG
Sbjct: 152  RLDSYARTVSLPSSCAGAGTSCLISGWGNTSSSGSNYPDRLMCLNAPILSDTSCRNSYPG 211

Query: 182  KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHI 241
            +I+ +M CAG ++ G DSCQGDSGGP+VC G+L+G+VSWG   C   + KPGVYT VC +
Sbjct: 212  QISTNMFCAGFLEGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRNKPGVYTKVCNYN 270

Query: 242  RWIQNIL 248
             W+++ +
Sbjct: 271  SWLRDTM 277


>gi|4389387|pdb|1A0J|D  Chain D, Crystal Structure Of A Non-Psychrophilic Trypsin
          Cold-Adapted Fish Species.
 gi|4389386|pdb|1A0J|C  Chain C, Crystal Structure Of A Non-Psychrophilic Trypsin Fr
          Cold-Adapted Fish Species.
 gi|4389385|pdb|1A0J|B  Chain B, Crystal Structure Of A Non-Psychrophilic Trypsin Fr
          Cold-Adapted Fish Species.
 gi|4389384|pdb|1A0J|A  Chain A, Crystal Structure Of A Non-Psychrophilic Trypsin Fr
          Cold-Adapted Fish Species.
         Length = 223

 Score =  207 bits (528), Expect = 2e-52
 Identities = 96/222 (43%), Positives = 138/222 (62%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G   C K+S   +QA+L   SG+   CGG LI     WV++AAHC K   +QV LG+HN+    E
Sbjct: 1    IVGGYECRKNSASYQASLQ-SGYHFCGGSLISSTWVVSAAHCYKSRIQVRLGEHNIAVNE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ I   + I+HP YN    DNDIM++ L   P    +   +   + L + C+     C +
Sbjct: 60   GTEQFIDSVKVIMHPSYNSRNLDNDIMLIKLSKPASLNSYVSTVALPSSCASSGTRCLVS 119

Query: 149  GWGKME--NGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG +    + ++PDT++C D+ ++    C   AYPG+IT +M CAG M+ G DSCQGDSGG
Sbjct: 120  GWGNLSGSSSNYPDTLRCLDLPILSSSSCNSAYPGQITSNMFCAGFMEGGKDSCQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG   C   + KPGVYT VC +   WI + +
Sbjct: 180  PVVCNGQLQGVVSWG-YGCAQRNKPGVYTKVCNYRSWISSTM 220


>gi|2392548|pdb|1TAW|A  Chain A, Bovine Trypsin Complexed To Appi
         Length = 223
```

```
 Score =  207 bits (528), Expect = 2e-52
 Identities = 96/222 (43%), Positives = 139/222 (62%), Gaps = 4/222 (1%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1   IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ IS  ++IVHP YN  T +NDIM++ LK+    + ++  + L   C+     C I
Sbjct: 60  GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K     +PD ++C    ++    C+ AYPG+IT +M CAG ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSTSSCKSAYPGQITSNMFCAGYLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG   C  K KPGVYT VC ++ WI+  +
Sbjct: 180 PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220
```

>gi|60593451|pdb|1S0R|A Chain A, Bovine Pancreatic Trypsin Inhibited With Benzam:
Atomic Resolution

gi|60593450|pdb|1S0Q|A Chain A, Native Bovine Pancreatic Trypsin

gi|49258809|pdb|1RXP|A Chain A, Structure Of Trypsin (Orthorhombic) With 1-(4-Tert
Butylcarbamoyl- Piperazine-1-Carbonyl)-3-(3-Guanidino-
Propyl)-4-Oxo-Azetidine-2-Carboxylic Acid

gi|49258395|pdb|1OX1|A Chain A, Crystal Structure Of The Bovine Trypsin Complex Wi
Synthetic 11 Peptide Inhibitor

gi|48425172|pdb|1P2K|A Chain A, Structural Consequences Of Accommodation Of Four N
Cognate Amino-Acid Residues In The S1 Pocket Of Bovine
Trypsin And Chymotrypsin

gi|48425170|pdb|1P2J|A Chain A, Structural Consequences Of Accommodation Of Four N
Cognate Amino-Acid Residues In The S1 Pocket Of Bovine
Trypsin And Chymotrypsin

gi|48425168|pdb|1P2I|A Chain A, Structural Consequences Of Accommodation Of Four N
Cognate Amino-Acid Residues In The S1 Pocket Of Bovine
Trypsin And Chymotrypsin

gi|37926888|pdb|1NC6|A Chain A, Potent, Small Molecule Inhibitors Of Human Mast Ce
Tryptase. Anti-Asthmatic Action Of A Dipeptide-Based
Transition State Analogue Containing Benzothiazole
Ketone

gi|34810041|pdb|1O3O|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M
Binding Of Active Site-Directed Serine Protease
Inhibitors

gi|34810040|pdb|1O3N|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M
Binding Of Active Site-Directed Serine Protease
Inhibitors

gi|34810039|pdb|1O3M|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M
Binding Of Active Site-Directed Serine Protease
Inhibitors

gi|34810038|pdb|1O3L|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M
Binding Of Active Site-Directed Serine Protease
Inhibitors

gi|34810037|pdb|1O3K|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M

Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810036|pdb|1O3J|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810035|pdb|1O3I|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810034|pdb|1O3H|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810033|pdb|1O3G|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810032|pdb|1O3F|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810031|pdb|1O3E|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810030|pdb|1O3D|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810029|pdb|1O3C|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810028|pdb|1O3B|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810027|pdb|1O3A|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810026|pdb|1O39|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810025|pdb|1O38|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810024|pdb|1O37|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810023|pdb|1O36|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810022|pdb|1O35|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810021|pdb|1O34|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810020|pdb|1O33|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810019|pdb|1O32|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M

Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810018|pdb|1031|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810017|pdb|1030|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810016|pdb|102Z|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810015|pdb|102Y|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810014|pdb|102X|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810013|pdb|102W|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810012|pdb|102V|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810011|pdb|102U|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810010|pdb|102T|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810009|pdb|102S|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810008|pdb|102R|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|34810007|pdb|102Q|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|31615754|pdb|102P|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|31615753|pdb|102O|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|31615752|pdb|102N|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|31615751|pdb|102M|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|31615750|pdb|102L|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M Binding Of Active Site-Directed Serine Protease Inhibitors

gi|31615749|pdb|102K|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M

Binding Of Active Site-Directed Serine Protease
Inhibitors

gi|31615748|pdb|1O2J|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M
Binding Of Active Site-Directed Serine Protease
Inhibitors

gi|31615747|pdb|1O2I|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M
Binding Of Active Site-Directed Serine Protease
Inhibitors

gi|31615746|pdb|1O2H|A Chain A, Elaborate Manifold Of Short Hydrogen Bond Arrays M
Binding Of Active Site-Directed Serine Protease
Inhibitors

gi|30750054|pdb|1OYQ|A Chain A, Trypsin Inhibitor Complex

gi|28948739|pdb|1N6Y|A Chain A, Rip-Phasing On Bovine Trypsin

gi|28948738|pdb|1N6X|A Chain A, Rip-Phasing On Bovine Trypsin

gi|3891399|pdb|1XUJ| Trypsin-Keto-Babim-Zn+2, Ph 8.2

gi|20663566|pdb|1GJ6|A Chain A, Engineering Inhibitors Highly Selective For The S1
Of Ser190 Trypsin-Like Serine Protease Drug Targets

gi|20149797|pdb|1EB2|A Chain A, Trypsin Inhibitor Complex (Bpo)

gi|17942817|pdb|1K1I|A Chain A, Bovine Trypsin-Inhibitor Complex

gi|17942816|pdb|1K1J|A Chain A, Bovine Trypsin-Inhibitor Complex

gi|17942815|pdb|1K1L|A Chain A, Bovine Trypsin-Inhibitor Complex

gi|17942814|pdb|1K1M|A Chain A, Bovine Trypsin-Inhibitor Complex

gi|17942813|pdb|1K1N|A Chain A, Bovine Trypsin-Inhibitor Complex

gi|17942812|pdb|1K1O|A Chain A, Bovine Trypsin-Inhibitor Complex

gi|17942811|pdb|1K1P|A Chain A, Bovine Trypsin-Inhibitor Complex

gi|16975154|pdb|1G36|A Chain A, Trypsin Inhibitor Complex

gi|15826250|pdb|1JIR|A Chain A, Crystal Structure Of Trypsin Complex With Amylamin
Cyclohexane

gi|15988427|pdb|1J8A|A Chain A, Crystal Structure Of Benzamidine Inhibited Bovine
Pancreatic Trypsin At 105k To 1.21a Resolution From
Laboratory Source With High Number Of Waters Modelled

gi|12084709|pdb|1G9I|E Chain E, Crystal Structure Of Beta-Trysin Complex In Cycloh

gi|13399519|pdb|1EJM|E Chain E, Crystal Structure Of The Bpti Ala16leu Mutant In C
With Bovine Trypsin

gi|13399517|pdb|1EJM|C Chain C, Crystal Structure Of The Bpti Ala16leu Mutant In C
With Bovine Trypsin

gi|13399515|pdb|1EJM|A Chain A, Crystal Structure Of The Bpti Ala16leu Mutant In C
With Bovine Trypsin

gi|10120745|pdb|1QL8|A Chain A, Factor Xa Specific Inhibitor In Complex With Bovin
Trypsin

gi|10120744|pdb|1QL7|A Chain A, Factor Xa Specific Inhibitor In Complex With Bovin
Trypsin

gi|9954886|pdb|1C9T|F Chain F, Complex Of Bdellastasin With Bovine Trypsin

gi|9954885|pdb|1C9T|E Chain E, Complex Of Bdellastasin With Bovine Trypsin

gi|9954884|pdb|1C9T|D Chain D, Complex Of Bdellastasin With Bovine Trypsin

gi|9954883|pdb|1C9T|C Chain C, Complex Of Bdellastasin With Bovine Trypsin

gi|9954882|pdb|1C9T|B Chain B, Complex Of Bdellastasin With Bovine Trypsin

gi|9954881|pdb|1C9T|A Chain A, Complex Of Bdellastasin With Bovine Trypsin

gi|8569655|pdb|1D6R|A Chain A, Crystal Structure Of Cancer Chemopreventive Bowman-

Inhibitor In Ternary Complex With Bovine Trypsin At 2.3
A Resolution. Structural Basis Of Janus-Faced Serine
Protease Inhibitor Specificity

gi|8569286|pdb|1F2S|E Chain E, Crystal Structure Of The Complex Formed Between Bov
Beta- Trypsin And Mcti-A, A Trypsin Inhibitor Of Squash
Family At 1.8 A Resolution

gi|5107687|pdb|1SBW|A Chain A, Crystal Structure Of Mung Bean Inhibitor Lysine Act
Fragment Complex With Bovine Beta-Trypsin At 1.8a
Resolutio

gi|7767179|pdb|1QA0|A Chain A, Bovine Trypsin 2-Aminobenzimidazole Complex

gi|7766894|pdb|1QB6|A Chain A, Bovine Trypsin 3,3'-[3,5-Difluoro-4-Methyl-2, 6-
Pyridinediylbis(Oxy)]bis(Benzenecarboximidamide)
(Zk-805623 Complex

gi|7766893|pdb|1QB1|A Chain A, Bovine Trypsin With 1-[2-[5-[amino(Imino)methyl]-2-
Hydroxyphenoxy]-6-[3-(4,
5-Dihydro-1-Methyl-1h-Imidazol-2-Yl
Phenoxy]pyridin-4-Yl]piperidine-3-Carboxylic Acid (Zk-
806974)

gi|7766880|pdb|1QB9|A Chain A, Bovine Trypsin
7-[[2-[[1-(1-Iminoethyl)piperidin-4-Yl]oxy]-
9h-Carbozol-9-Yl] Methyl]naphthalene-2-Carboximidamide
(Zk- 806450) Complex

gi|7766865|pdb|1QBO|A Chain A, Bovine Trypsin
7-[[6-[[1-(1-Iminoethyl)piperidin-4-Yl]oxy]-
2-Methyl-Benzimidazol-1-Yl]methyl]naphthalene-2-
Carboximidamid Zk-806711 Inhibitor Complex

gi|7766864|pdb|1QBN|A Chain A, Bovine Trypsin 2-[amino(Imino)methyl]-2-Hydroxyphen
[3-(4,5-Dihydro-1h-Imidazol-2-Yl)phenoxy]pyridine-4-
Carboxylic Acid (Zk-806688) Complex

gi|4699788|pdb|2BZA|A Chain A, Bovine Pancreas Beta-Trypsin In Complex With Benzyl

gi|4699733|pdb|1CE5|A Chain A, Bovine Pancreas Beta-Trypsin In Complex With Benzam

gi|7546600|pdb|3BTW|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti

gi|7546598|pdb|3BTT|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti

gi|7546596|pdb|3BTQ|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti

gi|7546594|pdb|3BTM|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti

gi|7546592|pdb|3BTK|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti

gi|7546590|pdb|3BTH|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti

gi|7546588|pdb|3BTG|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti

gi|7546586|pdb|3BTF|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti.

gi|7546584|pdb|3BTD|E Chain E, The Crystal Structures Of The Complexes Between The
Beta-Trypsin And Ten P1 Variants Of Bpti.

gi|7546570|pdb|3BTE|E Chain E, The Crystal Structures Of The Complexes Between Bov
Beta- Trypsin And Ten P1 Variants Of Bpti.

gi|5107649|pdb|1QCP|A Chain A, Crystal Structure Of The Rwj-51084 Bovine Pancreati
Trypsin At 1.8 A

gi|6980531|pdb|2BTC|E Chain E, Bovine Trypsin In Complex With Squash Seed Inhibito (Cucurbita Pepo Trypsin Inhibitor Ii)

gi|6729840|pdb|2TIO|A Chain A, Low Packing Density Form Of Bovine Beta-Trypsin In Cyclohexane

gi|6729821|pdb|1TIO|A Chain A, High Packing Density Form Of Bovine Beta-Trypsin In Cyclohexane

gi|5822405|pdb|1SFI|A Chain A, High Resolution Structure Of A Potent, Cyclic Prote Inhibitor From Sunflower Seeds

gi|5542502|pdb|1YYY|1 Chain 1, Trypsin Inhibitors With Rigid Tripeptidyl Aldehydes

gi|3891978|pdb|1AUJ| Bovine Trypsin Complexed To Meta-Cyano-Benzylic Inhibitor

gi|3891400|pdb|1XUK| Trypsin-Babim-Sulfate, Ph 5.9

gi|3891398|pdb|1XUI| Trypsin-Keto-Babim, Zn+2-Free, Ph 8.2

gi|3891397|pdb|1XUH| Trypsin-Keto-Babim-Co+2, Ph 8.2

gi|4139602|pdb|1XUG| Trypsin-Babim-Zn+2, Ph 8.2

gi|4139601|pdb|1XUF| Trypsin-Babim-Zn+2, Ph 8.2

gi|4139819|pdb|1BJV| Beta-Trypsin Complexed With Appu

gi|4139818|pdb|1BJU| Beta-Trypsin Complexed With Acpu

gi|4389362|pdb|1AZ8| Bovine Trypsin Complexed To Bis-Phenylamidine Inhibitor

gi|2624542|pdb|1MTW| Factor Xa Specific Inhibitor In Complex With Bovine Trypsin

gi|2624541|pdb|1MTV| Factor Xa Specific Inhibitor In Complex With Bovine Trypsin

gi|2624540|pdb|1MTU| Factor Xa Specific Inhibitor In Complex With Bovine Trypsin

gi|2392460|pdb|1MTS| Factor Xa Specific Inhibitor In Complex With Bovine Trypsin

gi|1827632|pdb|1MAY| Beta-Trypsin Phosphonate Inhibited

gi|1827633|pdb|1MAX| Beta-Trypsin Phosphonate Inhibited

gi|1827639|pdb|1JRT|A Chain A, Hemiacetal Complex Between Leupeptin And Trypsin

gi|1827641|pdb|1JRS|A Chain A, Hemiacetal Complex Between Leupeptin And Trypsin

gi|2982034|pdb|1AQ7| Trypsin With Inhibitor Aeruginosin 98-B

gi|230914|pdb|3PTN| Trypsin (Trigonal, 2.4 M Ammonium Sulfate) (E.C.3.4.21.4)

gi|230913|pdb|3PTB| Beta-Trypsin (Benzamidine Inhibited) At pH7 (E.C.3.4.21.4)

gi|230679|pdb|2PTN| Trypsin (Orthorhombic, 2.4 M Ammonium Sulfate) (E.C.3.4.21.4)

gi|230677|pdb|2PTC|E Chain E, Beta-Trypsin (E.C.3.4.21.4) Complex With Pancreatic Trypsin Inhibitor

gi|996178|pdb|1TYN| Beta Trypsin Complexed With Cyclotheonamide A

gi|1000005|pdb|1TPS| Trypsin Complexed With Inhibitor A90720a

gi|230378|pdb|1TPP| Beta-Trypsin (E.C.3.4.21.4) Complex With P-Amidino-Phenyl-Pyr (Appa)

gi|230377|pdb|1TPO| Beta-Trypsin (Orthorhombic) At pH5.0 (E.C.3.4.21.4)

gi|230372|pdb|1TPA|E Chain E, Anhydro-Trypsin (E.C.3.4.21.4) Complex With Pancreat Trypsin Inhibitor

gi|230361|pdb|1TLD| Beta-Trypsin (Orthorhombic) At pH 5.3 (E.C.3.4.21.4)

gi|230338|pdb|1TAB|E Chain E, Trypsin (E.C.3.4.21.4) Complex With Bowman-Birk Inhi (AB-I)

gi|576271|pdb|1SMF|E Chain E, Trypsin (E.C.3.4.21.4) Complexed With Bowman-Birk Inhibitor

gi|494471|pdb|1PPH|E Chain E, Trypsin (E.C.3.4.21.4) Complex With Noncovalently Bo 3-Tapap

gi|494465|pdb|1PPE|E Chain E, Trypsin (E.C.3.4.21.4) Complex With (Cucurbita Maxim Trypsin Inhibitor (Cmti-I)

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gi|494464|pdb|1PPC|E  S Chain E, Trypsin (E.C.3.4.21.4) Complex With Noncovalently Bo
          Napap
gi|494034|pdb|1GBT|   S Beta-Trypsin (E.C.3.4.21.4) Guanidinobenzoylated At Serine 19
          5.5)
         Length = 223

 Score =  207 bits (527), Expect = 2e-52
 Identities = 96/222 (43%), Positives = 139/222 (62%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1    IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ IS  ++IVHP YN  T +NDIM++ LK+    + ++  + L   C+     C I
Sbjct: 60   GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K     +PD ++C     ++    C+ AYPG+IT +M CAG ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG   C  K KPGVYT VC ++ WI+  +
Sbjct: 180 PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220


>gi|6981132|ref|NP_036725.1|  G kallikrein 7 [Rattus norvegicus]
gi|92889|pir||A31136   tissue kallikrein (EC 3.4.21.35) 7 precursor, submandibular - r
gi|547790|sp|P36373|KLK7_RAT  G Glandular kallikrein 7, submandibular/renal precursor
          kallikrein) (RGK-7) (RSKG-7) (Kallikrein-related protein
          K1) (Esterase B) (Proteinase A)
gi|205000|gb|AAA41461.1|  G kallikrein
         Length = 261

 Score =  207 bits (527), Expect = 2e-52
 Identities = 94/237 (39%), Positives = 140/237 (59%), Gaps = 13/237 (5%)

Query: 26   QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
            Q +V+ G  C K+S P+Q ALY+    LCGGVLIDP WV+TAAHC   N QV LG++NL
Sbjct: 22   QSRVIGGYKCEKNSQPWQVALYSFTKYLCGGVLIDPSWVITAAHCSSNNYQVWLGRNNLL 81

Query: 86   QTETFQRQISVDRTIVHPRYNP-----------ETHDNDIMMVHLKNPVKFSKKIQPLPL 134
            + E F +   V ++  HP Y P            + H ND+M++HL   P   +  ++ + L
Sbjct: 82   EDEPFAQHRLVSQSFPHPDYKPFLMRNHTRKPGDDHSNDLMLLHLSQPADITDGVKVIDL 141

Query: 135  KNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGD 192
              +  +     C   GWG  +     +FPD +QC ++HL+  E+C +AY  K+T  M+CAG+
Sbjct: 142  PTEEPKVGSTCLASGWGSTKPLIWEFPDDLQCVNIHLLSNEKCIKAYKEKVTDLMLCAGE 201

Query: 193  MKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
            ++ G D+C GDSGGPL+C G L+G+ SWG +PC     P +YT +     WI+ +++
Sbjct: 202  LEGGKDTCTGDSGGPLLCDGVLQGITSWGSVPCAKTNMPAIYTKLIKFTSWIKEVMK 258


>gi|2358071|gb|AAB69043.1|   trypsinogen 5 [Mus musculus]
         Length = 246
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Score =  207 bits (527), Expect = 2e-52
Identities = 97/230 (42%), Positives = 142/230 (61%), Gaps = 4/230 (1%)

Query: 23   SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKH 82
             +    +K+V G   C K S P+Q +L         CGG LI+ QWVL+AAHC K   LQV LG+H
Sbjct: 18   ANSDDKIVGGYTCPKHSVPYQVSLNDGISHQCGGSLINDQWVLSAAHCYK-RLQVRLGEH 76

Query: 83   NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
             N+    E  ++ I   ++ I HP YN +T DNDIM++ LK+P    + ++   + L   C+  N
Sbjct: 77   NIDVLEGGEQFIDAEKIIRHPDYNKDTVDNDIMLIKLKSPAILNSQVSTVSLPRSCASTN 136

Query: 143  PNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
               C + GWG    +  G +P   +QC +  ++    C+++YPG+IT +M C G ++ G DSC
Sbjct: 137  AQCLVSGWGNTVSIGGKYPALLQCLEAPVLSASSCKKSYPGQITSNMFCLGFLEGGKDSC 196

Query: 201  QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
              GDSGGP+VC G ++G+VSWG + C   + KPGVYT VC ++ WIQ   + N
Sbjct: 197  DGDSGGPVVCNGEIQGIVSWGSV-CAMRGKPGVYTKVCNYLSWIQETMAN 245
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>gi|22652265|gb|AAN03662.1| G kallikrein 7 long variant protein [Homo sapiens]
gi|21327705|ref|NP_644806.1| G stratum corneum chymotryptic enzyme preproprotein [Ho
gi|4826950|ref|NP_005037.1| G stratum corneum chymotryptic enzyme preproprotein [Hom
gi|14582758|gb|AAK69624.1| G stratum corneum chymotryptic enzyme [Homo sapiens]
gi|532504|gb|AAC37551.1| G stratum corneum chymotryptic enzyme
gi|11244765|gb|AAG33360.1| G stratum corneum chymotryptic enzyme [Homo sapiens]
gi|1082780|pir||A53968 serine proteinase SCCE precursor - human
gi|5733684|gb|AAD49718.1| G stratum corneum chymotryptic enzyme [Homo sapiens]
gi|1710878|sp|P49862|KLK7_HUMAN G Kallikrein 7 precursor (Stratum corneum chymotrypt
(hSCCE)
Length = 253

```
Score =  207 bits (526), Expect = 3e-52
Identities = 96/247 (38%), Positives = 140/247 (56%), Gaps = 4/247 (1%)

Query: 5    MLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
             +L +++L L L L  +      + +K++ G PC + SHP+Q AL +    L CGGVL++ +WV
Sbjct: 6    LLPLQILLLSLALETAGEEAQGDKIIDGAPCARGSHPWQVALLSGNQLHCGGVLVNERWV 65

Query: 65   LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
             LTAAHCK      V LG   L        ++I    ++  HP Y+ +TH ND+M+V L +  +
Sbjct: 66   LTAAHCKMNEYTVHLGSDTLGDRRA--QRIKASKSFRHPGYSTQTHVNDLMLVKLNSQAR 123

Query: 125  FSKKIQPLPLKNDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGK 182
             S  ++ + L + C       C + GWG    + D  FP  + C DV L+   + C + Y
Sbjct: 124  LSSMVKKVRLPSRCEPPGTTCTVSGWGTTTSPDVTFPSDLMCVDVKLISPQDCTKVYKDL 183

Query: 183  ITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
             +  SM+CAG       ++C GDSGGPLVC G L+GLVSWG  PCG    PGVYT VC    +
Sbjct: 184  LENSMLCAGIPDSKKNACNGDSGGPLVCRGTLQGLVSWGTFPCGQPNDPGVYTQVCKFTK 243

Query: 243  WIQNILR 249
             WI + ++
Sbjct: 244  WINDTMK 250
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>gi|51094518|gb|EAL23773.1|  protease, serine, 1 (trypsin 1) [Homo sapiens]
 gi|4506145|ref|NP_002760.1|  protease, serine, 1 preproprotein [Homo sapiens]
 gi|88941|pir||A25852  trypsin (EC 3.4.21.4) I precursor [validated] - human
 gi|1552515|gb|AAC80207.1|  trypsinogen A [Homo sapiens]
 gi|136408|sp|P07477|TRY1_HUMAN  Trypsin I precursor (Cationic trypsinogen)
 gi|521216|gb|AAA61231.1|  trypsinogen
 gi|224981|prf||1205235A  trypsinogen I
          Length = 247

 Score =  207 bits (526), Expect = 3e-52
 Identities = 102/249 (40%), Positives = 155/249 (62%), Gaps = 10/249 (4%)

Query: 2   PMKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDP 61
           P+ +LT    AL       +A  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+
Sbjct: 3   PLLILTFVAAAL------AAPFDDDDKIVGGYNCEENSVPYQVSL-NSGYHFCGGSLINE 55

Query: 62  QWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKN 121
           QWV++A HC K  +QV LG+HN+    E  ++ I+  + I HP+Y+ +T +NDIM++ L +
Sbjct: 56  QWVVSAGHCYKSRIQVRLGEHNIEVLEGNEQFINAAKIIRHPQYDRKTLNNDIMLIKLSS 115

Query: 122 PVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAY 179
              + ++  + L           C I GWG   +   D+PD +QC D  ++ + +CE +Y
Sbjct: 116 RAVINARVSTISLPTAPPATGTKCLISGWGNTASSGADYPDELQCLDAPVLSQAKCEASY 175

Query: 180 PGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCT 239
           PGKIT +M C G ++ G DSCQGDSGGP+VC G+L+G+VSWGD  C  K KPGVYT V
Sbjct: 176 PGKITSNMFCVGFLEGGKDSCQGDSGGPVVCNGQLQGVVSWGD-GCAQKNKPGVYTKVYN 234

Query: 240 HIRWIQNIL 248
           +++WI+N +
Sbjct: 235 YVKWIKNTI 243


>gi|230196|pdb|1NTP|  Modified Beta Trypsin (Monoisopropylphosphoryl Inhibited)
           (E.C.3.4.21.4) (Neutron Data)
          Length = 223

 Score =  207 bits (526), Expect = 3e-52
 Identities = 96/222 (43%), Positives = 138/222 (62%), Gaps = 4/222 (1%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
           +V G  C  ++ P+Q +L  SG+  CGG LID QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1   IVGGYTCGANTVPYQVSL-NSGYHFCGGSLIDSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
             ++ IS  ++IVHP Y+  T +NDIM++ LK+        ++  + L   C+     C I
Sbjct: 60  GNEQFISASKSIVHPSYDSNTLNNDIMLIKLKSAASLDSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
           GWG  K     +PD ++C   ++    C+ AYPG+IT +M CAG ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           P+VC G+L+G+VSWG   C  K KPGVYT VC ++ WI+  +
Sbjct: 180 PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220
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>gi|27710074|ref|XP_231718.1|  similar to Trypsin V-A precursor [Rattus norvegicus
 gi|57413|emb|CAA41751.1|   trypsin V a-form [Rattus rattus]
 gi|92926|pir||JQ1471   trypsin (EC 3.4.21.4) V precursor, a-form - rat
 gi|418136|sp|P32821|TRYA_RAT   Trypsin V-A precursor
          Length = 246

 Score =  206 bits (525), Expect = 4e-52
 Identities = 99/229 (43%), Positives = 141/229 (61%), Gaps = 4/229 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             +  +++V G  C + S P+Q +L     H+ CGG LI  QWVL+AAHC   P LQV LG+HN
Sbjct: 20   DNDDRIVGGYTCQEHSVPYQVSLNAGSHI-CGGSLITDQWVLSAAHCYHPQLQVRLGEHN 78

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             + + E  ++ I   + I+HP Y+  T DNDIM++ LK+P    + K+  +PL    C
Sbjct: 79   IYEIEGAEQFIDAAKMILHPDYDKWTVDNDIMLIKLKSPATLNSKVSTIPLPQYCPTAGT 138

Query: 144  NCQILGWGKMENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQG 202
              C + GWG ++ G + P  +QC D  ++     C +AYP +IT +M C G ++ G DSCQ
Sbjct: 139  ECLVSGWGVLKFGFESPSVLQCLDAPVLSDSVCHKAYPRQITNNMFCLGFLEGGKDSCQY 198

Query: 203  DSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWI-QNILRN 250
             DSGGP+VC G ++G+VSWGD  C   + KPGVYT VC ++ WI Q I  N
Sbjct: 199  DSGGPVVCNGEVQGIVSWGD-GCALEGKPGVYTKVCNYLNWIHQTIAEN 246


>gi|67551|pir||TRDGC   trypsin (EC 3.4.21.4) precursor, cationic - dog
 gi|136406|sp|P06871|TRY1_CANFA   Cationic trypsin precursor
 gi|164097|gb|AAA30900.1|   cationic trypsinogen precursor
          Length = 246

 Score =  206 bits (525), Expect = 4e-52
 Identities = 96/227 (42%), Positives = 142/227 (62%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG++N
Sbjct: 19   DDDDKIVGGYTCSRNSVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSRIQVRLGEYN 77

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +  +E  ++ I+  + I HPRYN  T DNDIM++ L +P    + ++  + L   C
Sbjct: 78   IAVSEGGEQFINAAKIIRHPRYNANTIDNDIMLIKLSSPATLNSRVSAIALPKSCPAAGT 137

Query: 144  NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG  ++    ++PD +QC    ++     C  AYPG+I+ +M+C G M+ G DSCQ
Sbjct: 138  QCLISGWGNTQSIGQNYPDVLQCLKAPILSDSVCRNAYPGQISSNMMCLGYMEGGKDSCQ 197

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G L+G+VSWG   C  K KPGV   VC ++ WIQ +
Sbjct: 198  GDSGGPVVCNGELQGVVSWG-AGCAQKGKPGVSPKVCKYVSWIQQTI 243


>gi|10835849|pdb|1FNI|A  Chain A, Crystal Structure Of Porcine Beta Trypsin With (
            Polydocanol
 gi|10835848|pdb|1FN6|A  Chain A, Crystal Structure Of Porcine Beta Trypsin With 0.1
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```
          Polydocanol
gi|10835846|pdb|1FMG|A   Chain A, Crystal Structure Of Porcine Beta Trypsin With 0.0
          Polydocanol
gi|9257116|pdb|1QQU|A   Chain A, Crystal Structure Of Porcine Beta Trypsin With Boun
          Acetate Ion
gi|494360|pdb|1MCT|A   Chain A, Trypsin (E.C.3.4.21.4) Complexed With Inhibitor From
          Bitter Gourd
         Length = 223

 Score =  206 bits (525), Expect = 4e-52
 Identities = 94/222 (42%), Positives = 136/222 (61%), Gaps = 4/222 (1%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C  +S P+Q +L +   H  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1   IVGGYTCAANSIPYQVSLNSGSHF-CGGSLINSQWVVSAAHCYKSRIQVRLGEHNIDVLE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ I+   + I HP +N  T DNDIM++ L +P   + ++  + L   C+      C I
Sbjct: 60  GNEQFINAAKIITHPNFNGNTLDNDIMLIKLSSPATLNSRVATVSLPRSCAAAGTECLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K      +P  +QC     ++     C+ +YPG+IT +M+C G ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGSSYPSLLQCLKAPVLSNSSCKSSYPGQITGNMICVGFLQGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG    C  K KPGVYT VC ++ WIQ  +
Sbjct: 180 PVVCNGQLQGIVSWG-YGCAQKNKPGVYTKVCNYVNWIQQTI 220


>gi|576019|pdb|1BRC|E   Chain E, Trypsin (E.C.3.4.21.4) Variant (D189g,G226d) Comp:
          With Amyloid Beta-Protein Precursor Inhibitor Domain
          (Appi)
gi|576017|pdb|1BRB|E   Chain E, Trypsin (E.C.3.4.21.4) Variant (D189g, G226d) Comple
          With Bpti Variant (C5a, C55a)
gi|515094|pdb|1BRA|   Trypsin (E.C.3.4.21.4) Variant (D189g,G226d) Complexed With
          Benzamidine
         Length = 223

 Score =  206 bits (525), Expect = 4e-52
 Identities = 97/222 (43%), Positives = 145/222 (65%), Gaps = 4/222 (1%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1   IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ ++   + I HP ++ +T +NDIM++ L +PVK + ++  + L + C+      C I
Sbjct: 60  GNEQFVNAAKIIKHPNFDRKTLNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149 GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  + +G + PD +QC D  L+P+  CE +YPGKIT +MVC G ++ G  SCQGDSGG
Sbjct: 120 GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASYPGKITDNMVCVGFLEGGKGSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G L+G+VSWG    C    + P VYT VC ++ WIQ+ +
Sbjct: 180 PVVCNGELQGIVSWG-YGCALPDNPDVYTKVCNYVDWIQDTI 220
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>gi|45382399|ref|NP_990716.1|  trypsinogen [Gallus gallus]
 gi|2499862|sp|Q90627|TRY1_CHICK  Trypsin I-P1 precursor
 gi|603903|gb|AAA79912.1|  trypsinogen
          Length = 248

 Score =  206 bits (524), Expect = 5e-52
 Identities = 97/227 (42%), Positives = 140/227 (61%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             E+ +K+V G  C + + P+Q +L  SG+  CGG LI  QWVL+AAHC K ++QV LG++N
Sbjct: 21   EDDDKIVGGYSCARSAAPYQVSL-NSGYHFCGGSLISSQWVLSAAHCYKSSIQVKLGEYN 79

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             L   +  ++ IS  + I H  YN  T +NDIM++ L       +  +  +PL   C
Sbjct: 80   LAAQDGSEQTISSSKVIRHSGYNANTLNNDIMLIKLSKAATLNSYVNTVPLPTSCVTAGT 139

Query: 144  NCQILGWGK-MENGD-FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG  + +G  +PD +QC +   ++    QC  AYPG+IT +M+C G +   G DSCQ
Sbjct: 140  TCLISGWGNTLSSGSLYPDVLQCLNAPVLSSSQCSSAYPGRITSNMICIGYLNGGKDSCQ 199

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG + C   K  PGVYT VC ++ WI+   +
Sbjct: 200  GDSGGPVVCNGQLQGIVSWG-IGCAQKGYPGVYTKVCNYVSWIKTTM 245


>gi|51746022|ref|XP_355892.2|  RIKEN cDNA 2310008B01 [Mus musculus]
          Length = 405

 Score =  206 bits (524), Expect = 5e-52
 Identities = 96/231 (41%), Positives = 147/231 (63%), Gaps = 7/231 (3%)

Query: 25   EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNL 84
             ++EK+ +G  C+K+S P+Q  L+   +L CGGVL+D +WVLTAAHC+   + V LG+H+L
Sbjct: 176  DREKIYNGVECVKNSQPWQVGLFHGKYLRCGGVLVDRKWVLTAAHCRDKYV-VRLGEHSL 234

Query: 85   RQTETFQRQISVDRTIVHPRYNP--ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
             + +  ++       +I HP Y    + H++D+ ++ L  P+   ++ ++P+ L + C
Sbjct: 235  TKLDWTEQLRHTTFSITHPSYQGAYQNHEHDLRLLRLNRPIHLTRAVRPVALPSSCVTTG 294

Query: 143  PNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
               C + GWG         FPD +QC ++  V  E C   +PG++T++M+CAG  + G D+C
Sbjct: 295  AMCHVSGWGTTNKPWDPFPDRLQCLNLSTVSNETCRAVFPGRVTENMLCAGG-EAGKDAC 353

Query: 201  QGDSGGPLVCGGRLRGLVSWGDM-PCGSKEKPGVYTDVCTHIRWIQNILRN 250
             QGDSGGPLVCGG L+GLVSWG + PCG K  PGVYT VC +  WI+ ++RN
Sbjct: 354  QGDSGGPLVCGGVLQGLVSWGSVGPCGQKGIPGVYTKVCKYTDWIRIVIRN 404


 Score =  115 bits (287), Expect = 1e-24
 Identities = 65/155 (41%), Positives = 88/155 (56%), Gaps = 17/155 (10%)

Query: 14   CLVLAKSAW-SEEQEKVVHGG-----------PCLKDSHPFQAALYTSGHLLCGGVLIDP 61
             CL LA S   S +  K+++G                       CL  S P+QAAL    G LLCGGVL+ P
Sbjct: 10   CLTLALSEGISRDYPKILNGTNGTSGFLPGGYTCLPHSQPWQAALLIRGRLLCGGVLVHP 69
```

```
Query: 62   QWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPE----THDNDIMMV 117
            +WVLTAAHC+K      V LGKH L + E   ++ + V R+I HP Y        HD+DIM++
Sbjct: 70   KWVLTAAHCRKDGYTVHLGKHALGRVENGEQAMEVVRSIPHPEYQVTPTHLNHDHDIMLL 129

Query: 118  HLKNPVKFSKKIQPLPLK-NDCSEENPNCQILGWG 151
             LK+PV+ S   ++ L L  +DC       C++ GWG
Sbjct: 130  ELKSPVQLSSHVRTLKLSADDCLPTGTCCRVSGWG 164
```

>gi|34811715|pdb|1HJ9|A Chain A, Atomic Resolution Structures Of Trypsin Provide Into Structural Radiation Damage

gi|18655757|pdb|1GI5|A Chain A, A Novel Serine Protease Inhibition Motif Involving Multi- Centered Short Hydrogen Bonding Network At The Active Site

gi|18655754|pdb|1GI2|A Chain A, A Novel Serine Protease Inhibition Motif Involving Multi- Centered Short Hydrogen Bonding Network At The Active Site

gi|9955040|pdb|1C1N|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|18655758|pdb|1GI6|A Chain A, A Novel Serine Protease Inhibition Motif Involving Multi- Centered Short Hydrogen Bonding Network At The Active Site

gi|18655756|pdb|1GI4|A Chain A, A Novel Serine Protease Inhibition Motif Involving Multi- Centered Short Hydrogen Bonding Network At The Active Site

gi|18655755|pdb|1GI3|A Chain A, A Novel Serine Protease Inhibition Motif Involving Multi- Centered Short Hydrogen Bonding Network At The Active Site

gi|18655753|pdb|1GI1|A Chain A, A Novel Serine Protease Inhibition Motif Involving Multi- Centered Short Hydrogen Bonding Network At The Active Site

gi|18655752|pdb|1GI0|A Chain A, A Novel Serine Protease Inhibition Motif Involving Multi- Centered Short Hydrogen Bonding Network At The Active Site

gi|18655751|pdb|1GHZ|A Chain A, A Novel Serine Protease Inhibition Motif Involving Multi- Centered Short Hydrogen Bonding Network At The Active Site

gi|12084304|pdb|1C5V|A Chain A, Structural Basis For Selectivity Of A Small Molecu Binding, Sub-Micromolar Inhibitor Of Urokinase Type Plasminogen Activator

gi|12084303|pdb|1C5U|A Chain A, Structural Basis For Selectivity Of A Small Molecu Binding, Sub-Micromolar Inhibitor Of Urokinase Type Plasminogen Activator

gi|12084302|pdb|1C5T|A Chain A, Structural Basis For Selectivity Of A Small Molecu Binding, Sub-Micromolar Inhibitor Of Urokinase Type Plasminogen Activator

gi|12084301|pdb|1C5S|A Chain A, Structural Basis For Selectivity Of A Small Molecu Binding, Sub-Micromolar Inhibitor Of Urokinase Type Plasminogen Activator

gi|12084300|pdb|1C5R|A Chain A, Structural Basis For Selectivity Of A Small Molecu Binding, Sub-Micromolar Inhibitor Of Urokinase Type Plasminogen Activator

gi|12084299|pdb|1C5Q|A Chain A, Structural Basis For Selectivity Of A Small Molecu Binding, Sub-Micromolar Inhibitor Of Urokinase Type

Plasminogen Activator

gi|12084298|pdb|1C5P|A Chain A, Structural Basis For Selectivity Of A Small Molecu Binding, Sub-Micromolar Inhibitor Of Urokinase Type Plasminogen Activator

gi|9955065|pdb|1C2M|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955064|pdb|1C2L|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955063|pdb|1C2K|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955062|pdb|1C2J|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955061|pdb|1C2I|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955060|pdb|1C2H|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955059|pdb|1C2G|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955058|pdb|1C2F|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955057|pdb|1C2E|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955056|pdb|1C2D|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955046|pdb|1C1T|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955044|pdb|1C1R|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955043|pdb|1C1Q|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955042|pdb|1C1P|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955041|pdb|1C1O|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

gi|9955045|pdb|1C1S|A Chain A, Recruiting Zinc To Mediate Potent, Specific Inhibit Serine Proteases

Length = 223

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 Score =  206 bits (524), Expect = 5e-52
 Identities = 96/221 (43%), Positives = 138/221 (62%), Gaps = 4/221 (1%)

Query: 30   VHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTET 89
            V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+  E
Sbjct: 2    VGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVEG 60

Query: 90   FQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILG 149
             ++ IS  ++IVHP YN  T +NDIM++ LK+     + ++  + L   C+     C I G
Sbjct: 61   NEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLISG 120

Query: 150  WG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGP 207
            WG  K      +PD ++C     ++      C+ AYPG+IT +M CAG ++ G DSCQGDSGGP
Sbjct: 121  WGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQGDSGGP 180

Query: 208  LVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
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           +VC G+L+G+VSWG    C  K KPGVYT VC ++ WI+   +
Sbjct: 181 VVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220
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>gi|5441855|dbj|BAA82363.1| trypsinogen 2 [Paralichthys olivaceus]
Length = 238

Score = 206 bits (524), Expect = 5e-52
Identities = 95/234 (40%), Positives = 142/234 (60%), Gaps = 2/234 (0%)

```
Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPN 74
           ++L  +A++ E +K+V G  C   S P Q +L  SG+  CGG L++  WV++AAHC K
Sbjct: 4   ILLIGAAFATEDDKIVGGYECTPYSQPHQVSL-NSGYHFCGGSLVNENWVVSAAHCYKSR 62

Query: 75  LQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           ++V +G+HNLR  E  ++ IS  R I HP Y+    +NDIM++ L  P   ++ +QP+ L
Sbjct: 63  VEVRIGEHNLRVYEETEQFISSSRVIRHPNYSSYNINNDIMLIKLSEPATLNQYVQPVAL 122

Query: 135 KNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMK 194
               C+     C + GWG    +      +QC D+ ++    CE +YPG IT +M CAG ++
Sbjct: 123 PTSCAPAGTMCTVSGWGDTMSSTDSSRLQCLDLPILSERDCENSYPGMITNAMFCAGYLE 182

Query: 195 EGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            G DSCQGDSGGP+VC G+L+G+VSWG    C  ++ PGVY  VC  I W++  +
Sbjct: 183 GGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRDHPGVYAKVCIFIDWLERTM 235
```

>gi|12843871|dbj|BAB26143.1| G unnamed protein product [Mus musculus]
Length = 234

Score = 206 bits (524), Expect = 5e-52
Identities = 96/231 (41%), Positives = 147/231 (63%), Gaps = 7/231 (3%)

```
Query: 25  EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNL 84
           ++EK+ +G  C+K+S P+Q  L+   +L CGGVL+D +WVLTAAHC+   + V LG+H+L
Sbjct: 5   DREKIYNGVECVKNSQPWQVGLFHGKYLRCGGVLVDRKWVLTAAHCRDKYV-VRLGEHSL 63

Query: 85  RQTETFQRQISVDRTIVHPRYNP--ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
            + +  ++       +I HP Y    + H++D+ ++ L  P+  ++ ++P+ L + C
Sbjct: 64  TKLDWTEQLRHTTFSITHPSYQGAYQNHEHDLRLLRLNRPIHLTRAVRPVALPSSCVTTG 123

Query: 143 PNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
             C + GWG        FPD +QC ++  V  E C   +PG++T++M+CAG  + G D+C
Sbjct: 124 AMCHVSGWGTTNKPWDPFPDRLQCLNLSTVSNETCRAVFPGRVTENMLCAGG-EAGKDAC 182

Query: 201 QGDSGGPLVCGGRLRGLVSWGDM-PCGSKEKPGVYTDVCTHIRWIQNILRN 250
           QGDSGGPLVCGG L+GLVSWG + PCG K  PGVYT VC +  WI+ ++RN
Sbjct: 183 QGDSGGPLVCGGVLQGLVSWGSVGPCGQKGIPGVYTKVCKYTDWIRIVIRN 233
```

>gi|56611170|gb|AAH87830.1| G Hypothetical LOC496697 [Xenopus tropicalis]
gi|58332206|ref|NP_001011251.1| G hypothetical LOC496697 [Xenopus tropicalis]
Length = 249

Score = 206 bits (523), Expect = 6e-52
Identities = 94/248 (37%), Positives = 146/248 (58%), Gaps = 6/248 (2%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M +  L  +    +A    + +K+V G  C    S P+Q       +  + CGG L+ P+W+++A
Sbjct: 2    MPLWILLFLAVAAAAPLDDDKIVGGYECTPHSQPWQVYFTQNSQVFCGGSLVTPRWIISA 61

Query: 68   AHCKKPNLQVI--LGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKF 125
            AHC +P    ++   LG H+L + E   ++ I V+     H  Y  E +D+DIM+V L  P ++
Sbjct: 62   AHCYRPPKTLVAHLGDHDLTKEEGTEQHIQVEAAYKHSSYKDEAYDHDIMLVKLAKPAQY 121

Query: 126  SKKIQPLPLKNDCSEENPNCQILGWGKMEN---GDFPDTIQCADVHLVPREQCERAYPGK 182
            ++ +QP+P+    C  E    C + G+G + +    G+FPD +QC DV ++      C+ +  G
Sbjct: 122  NQYVQPIPVARSCPREGTECLVSGYGNLRSDHIGEFPDRLQCVDVPVLSDSSCKASCRGL 181

Query: 183  ITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
             T++M CAG ++ G DSCQ DSGGPLVC G L G+VSWG    C  +  PGVY  VC ++R
Sbjct: 182  FTENMFCAGFLEGGKDSCQVDSGGPLVCNGELYGVVSWG-WGCAQRNAPGVYAKVCNYLR 240

Query: 243  WIQNILRN 250
            W+QNI+ N
Sbjct: 241  WVQNIIEN 248
```

>gi|60599777|gb|AAT11803.2| pancreatic trypsinogen [Struthio camelus]
Length = 231

```
 Score =  206 bits (523), Expect = 6e-52
 Identities = 97/226 (42%), Positives = 141/226 (62%), Gaps = 4/226 (1%)

Query: 25   EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNL 84
            + +K+V G  C   S P+Q +L  +G+  CGG LI+ QWVL+AAHC K ++QV LG++N+
Sbjct: 5    DDDKIVGGYNCPAHSVPYQVSL-NAGYHFCGGSLINSQWVLSAAHCYKSSIQVRLGEYNI 63

Query: 85   RQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPN 144
               E  +    S    I HP+Y+    + DNDIM++ L +PV +S   +QP+ L + C +
Sbjct: 64   DVREDSEVVRSSAAVIRHPKYSSRSLDNDIMLIKLASPVAYSADVQPIALPSSCVKAGTK 123

Query: 145  CQILGWGK--MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQG 202
            C I GWG         FP+ +QC     ++     +C  AYPG+I+ +M+C G ++ G DSCQG
Sbjct: 124  CLISGWGNTLSSGSSFPEILQCLQAPVLSDRECRNAYPGEISSNMICVGFLEGGKDSCQG 183

Query: 203  DSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            DSGGP+VC G L+G+VSWG + C  K  PGVYT VC ++ WIQ  +
Sbjct: 184  DSGGPVVCDGTLQGIVSWG-IGCAQKGYPGVYTKVCNYVSWIQETI 228
```

>gi|11244763|gb|AAG33358.1| G stratum corneum trypsin-like serine protease [Homo sa
Length = 253

```
 Score =  206 bits (523), Expect = 6e-52
 Identities = 99/251 (39%), Positives = 151/251 (60%), Gaps = 5/251 (1%)

Query: 3    MKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTS-GHLLCGGVLIDP 61
            M +L    + AL L +  +    +   ++++G  C    + P+QAAL          L CG VL+ P
Sbjct: 1    MWVLCALITALLLGVTDARSDDSSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHP 60

Query: 62   QWVLTAAHCKKPNLQVILGKHNLRQT-ETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
            QW+LTAAHC+K      +V LG ++L      E+ Q+        ++I HP Y+     H ND+M++ L
```

```
Sbjct: 61   QWLLTAAHCRKKVFRVRLGHYSLSPVYESGQQMFQGVKSIPHPGYSHPGHSNDLMLIKLN 120

Query: 121  NPVKFSKKIQPLPLKNDCSEENPNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERA 178
               ++ +K ++P+ + + C      C + GWG  K     FP  +QC ++ ++ +++CE A
Sbjct: 121  RRIRPTKDVRPINVSSHCPSAGTKCLVSGWGTTKSPQVHFPKVLQCLNISVLSQKRCEDA 180

Query: 179  YPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVC 238
            YP +I   +M CAGD K G DSCQGDSGGP+VC G L+GLVSWGD PC     +PGVYT++C
Sbjct: 181  YPRQIDDTMFCAGD-KAGRDSCQGDSGGPVVCNGSLQGLVSWGDYPCARPNRPGVYTNLC 239

Query: 239  THIRWIQNILR 249
               +WIQ  ++
Sbjct: 240  KFTKWIQETIQ 250
```

>gi|2118087|pir||S55067 trypsin (EC 3.4.21.4) I precursor, pancreatic - chicken
Length = 248

Score = 206 bits (523), Expect = 6e-52
Identities = 102/248 (41%), Positives = 148/248 (59%), Gaps = 5/248 (2%)

```
Query: 3    MKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQ 62
            MK L + +  L + +A      E+ +K+V G  C + + P+Q +L  SG+  CGG LI  Q
Sbjct: 1    MKFLVL-VAFLGVAVAFPISDEDDDKIVGGYSCARSAAPYQVSL-NSGYHFCGGSLISSQ 58

Query: 63   WVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNP 122
            WVL+AAHC K ++QV LG++NL    +  ++ IS  + I H  YN  T +NDIM++ L
Sbjct: 59   WVLSAAHCYKSSIQVKLGEYNLAAQDGSEQTISSSKVIRHSGYNSNTLNNDIMLIKLSKA 118

Query: 123  VKFSKKIQPLPLKNDCSEENPNCQILGWGK-MENGD-FPDTIQCADVHLVPREQCERAYP 180
               +  +  +PL   C      C I GWG  + +G  +PD +QC +  ++   QC  AYP
Sbjct: 119  ATLNSYVNTVPLPTSCVTAGTTCLISGWGNTLSSGSLYPDVLQCLNAPVLSSSQCSSAYP 178

Query: 181  GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
            G+IT +M+C G +  G DSCQGDSGGP+VC G+L+G VSWG + C  K  PGVYT VC +
Sbjct: 179  GRITSNMICIGYLNGGKDSCQGDSGGPVVCNGQLQGFVSWG-IGCAQKGYPGVYTKVCNY 237

Query: 241  IRWIQNIL 248
            + WI+  +
Sbjct: 238  VSWIKTTM 245
```

>gi|2499863|sp|Q90628|TRY2_CHICK Trypsin I-P38 precursor
gi|603905|gb|AAA79913.1| G trypsinogen
Length = 248

Score = 206 bits (523), Expect = 6e-52
Identities = 102/248 (41%), Positives = 148/248 (59%), Gaps = 5/248 (2%)

```
Query: 3    MKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQ 62
            MK L + +  L + +A      E+ +K+V G  C + + P+Q +L  SG+  CGG LI  Q
Sbjct: 1    MKFLVL-VAFLGVAVAFPISDEDDDKIVGGYSCARSAAPYQVSL-NSGYHFCGGSLISSQ 58

Query: 63   WVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNP 122
            WVL+AAHC K ++QV LG++NL    +  ++ IS  + I H  YN  T +NDIM++ L
Sbjct: 59   WVLSAAHCYKSSIQVKLGEYNLAAQDGSEQTISSSKVIRHSGYNANTLNNDIMLIKLSKA 118
```

```
Query: 123 VKFSKKIQPLPLKNDCSEENPNCQILGWGK-MENGD-FPDTIQCADVHLVPREQCERAYP 180
              +  +  +PL   C      C I GWG  + +G  +PD +QC +  ++   QC  AYP
Sbjct: 119 ATLNSYVNTVPLPTSCVTAGTTCLISGWGNTLSSGSLYPDVLQCLNAPVLSSSQCSSAYP 178

Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
           G+IT +M+C G +  G DSCQGDSGGP+VC G+L+G VSWG + C  K  PGVYT VC +
Sbjct: 179 GRITSNMICIGYLNGGKDSCQGDSGGPVVCNGQLQGFVSWG-IGCAQKGYPGVYTKVCNY 237

Query: 241 IRWIQNIL 248
           + WI+  +
Sbjct: 238 VSWIKTTM 245
```

>gi|51247093|pdb|1H9I|E Chain E, Complex Of Eeti-Ii Mutant With Porcine Trypsin
gi|51247091|pdb|1H9H|E Chain E, Complex Of Eeti-Ii With Porcine Trypsin
gi|47169105|pdb|1S85|A Chain A, Porcine Trypsin Complexed With P-Hydroxymethyl Ben And Borate
gi|47169104|pdb|1S84|A Chain A, Porcine Trypsin Covalent Complex With 4-Amino Buta Borate And Ethylene Glycol
gi|47169103|pdb|1S83|A Chain A, Porcine Trypsin Complexed With 4-Amino Propanol
gi|47169102|pdb|1S82|A Chain A, Porcine Trypsin Complexed With Borate And Ethylene
gi|47169101|pdb|1S81|A Chain A, Porcine Trypsin With No Inhibitor Bound
gi|47169077|pdb|1S6H|A Chain A, Porcine Trypsin Complexed With Guanidine-3-Propano Inhibitor
gi|47169076|pdb|1S6F|A Chain A, Porcine Trypsin Covalent Complex With Borate And Guanidine- 3 Inhibitor
gi|47169075|pdb|1S5S|A Chain A, Porcine Trypsin Complexed With Guanidine-3-Propano Inhibitor
gi|40889515|pdb|1R0T|A Chain A, Crystal Structure Of Trypsin-Second Domain Of The Ovomucoid Turkey Egg White Inhibitor Complex
gi|58176994|pdb|1V6D|A Chain A, The Crystal Structure Of The Trypsin Complex With Synthetic Heterochiral Peptide
gi|13399521|pdb|1EJA|A Chain A, Structure Of Porcine Trypsin Complexed With Bdella An Antistasin-Type Inhibitor
gi|3891587|pdb|1AVX|A Chain A, Complex Porcine Pancreatic TrypsinSOYBEAN TRYPSIN Inhibitor, Tetragonal Crystal Form
gi|3891585|pdb|1AVW|A Chain A, Complex Porcine Pancreatic TrypsinSOYBEAN TRYPSIN Inhibitor, Orthorhombic Crystal Form
gi|2914483|pdb|1TFX|B Chain B, Complex Of The Second Kunitz Domain Of Tissue Facto Pathway Inhibitor With Porcine Trypsin
gi|2914482|pdb|1TFX|A Chain A, Complex Of The Second Kunitz Domain Of Tissue Facto Pathway Inhibitor With Porcine Trypsin
gi|3212563|pdb|1LDT|T Chain T, Complex Of Leech-Derived Tryptase Inhibitor With Po Trypsin
Length = 223

Score = 206 bits (523), Expect = 6e-52
Identities = 94/222 (42%), Positives = 136/222 (61%), Gaps = 4/222 (1%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
           +V G  C  +S P+Q +L +  H  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1   IVGGYTCAANSIPYQVSLNSGSHF-CGGSLINSQWVVSAAHCYKSRIQVRLGEHNIDVLE 59
```

```
Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ I+   + I HP +N  T DNDIM++ L +P    + ++   + L    C+      C I
Sbjct: 60   GNEQFINAAKIITHPNFNGNTLDNDIMLIKLSSPATLNSRVATVSLPRSCAAAGTECLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K       +P   +QC       ++      C+ +YPG+IT +M+C G ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGSSYPSLLQCLKAPVLSDSSCKSSYPGQITGNMICVGFLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG    C  K KPGVYT VC ++ WIQ  +
Sbjct: 180 PVVCNGQLQGIVSWG-YGCAQKNKPGVYTKVCNYVNWIQQTI 220
```

>gi|2392803|pdb|5PTP| Structure Of Hydrolase (Serine Proteinase)
Length = 223

```
 Score =  206 bits (523), Expect = 6e-52
 Identities = 95/222 (42%), Positives = 138/222 (62%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G   C   ++ P+Q +L   SG+   CGG LI+ QWV++AAHC K   +QV LG+ N+    E
Sbjct: 1    IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ IS   ++IVHP YN   T +NDIM++ LK+       + ++   + L    C+       C I
Sbjct: 60   GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K       +PD ++C       ++      C+ AYPG+IT +M CAG ++ G DSCQGD GG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAGYLEGGKDSCQGDXGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG    C  K KPGVYT VC ++ WI+  +
Sbjct: 180 PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220
```

>gi|33126535|gb|AAL14243.1| protease serine 4 isoform B [Homo sapiens]
Length = 261

```
 Score =  205 bits (522), Expect = 8e-52
 Identities = 95/227 (41%), Positives = 144/227 (63%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G   C ++S P+Q +L +  H  CGG LI  QWV++AAHC K   +QV LG+HN
Sbjct: 33   DDDDKIVGGYTCEENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKSRIQVRLGEHN 91

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             ++   E  ++ I+   + I HP+YN +T DNDIM++ L +P    + ++   + L
Sbjct: 92   IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTAPPAAGT 151

Query: 144 NCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG        D+PD ++C D   ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 152 ECLISGWGNTLSSGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 211

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+VC G+L+G+VSWG    C  K +PGVYT V  ++ WI++ +
Sbjct: 212 GDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 257
```

```
>gi|18777665|ref|NP_036002.1|  G kallikrein 7 [Mus musculus]
 gi|20380020|gb|AAH27823.1|  G Kallikrein 7 [Mus musculus]
 gi|14582804|gb|AAK69652.1|  G stratum corneum chymotryptic enzyme [Mus musculus]
 gi|26346272|dbj|BAC36787.1|  G unnamed protein product [Mus musculus]
 gi|14141577|dbj|BAB55604.1|  G thymopsin [Mus musculus]
 gi|26325426|dbj|BAC26467.1|  G unnamed protein product [Mus musculus]
          Length = 249

 Score =  205 bits (522), Expect = 8e-52
 Identities = 99/244 (40%), Positives = 139/244 (56%), Gaps = 6/244 (2%)

Query: 10  MLALCLVLAKSAWSE--EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            +L+L  VL   A      + E+++ G  C + SHP+Q AL      L CGGVL+D  WVLTA
Sbjct: 5   LLSLITVLLSLALETAGQGERIIDGYKCKEGSHPWQVALLKGNQLHCGGVLVDKYWVLTA 64

Query: 68  AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHCK     QV LG   +        ++I    ++   HP Y+ +TH NDIM+V L   PVK S
Sbjct: 65  AHCKMGQYQVQLGSDKIGDQSA--QKIKATKSFRHPGYSTKTHVNDIMLVRLDEPVKMSS 122

Query: 128 KIQPLPLKNDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGKITQ 185
            K++ + L    C       +C + GWG     + D  FP   + C+DV L+    +C++ Y    + +
Sbjct: 123 KVEAVQLPEHCEPPGTSCTVSGWGTTTSPDVTFPSDLMCSDVKLISSRECKKVYKDLLGK 182

Query: 186 SMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQ 245
            +M+CAG       ++C GDSGGPLVC     L+GLVSWG   PCG     PGVYT VC + RW+
Sbjct: 183 TMLCAGIPDSKTNTCNGDSGGPLVCNDTLQGLVSWGTYPCGQPNDPGVYTQVCKYKRWVM 242

Query: 246 NILR 249
              ++
Sbjct: 243 ETMK 246


>gi|93017|pir||A27207  tissue kallikrein (EC 3.4.21.35), prostatic - guinea pig
 gi|125173|sp|P12323|KLK2_CAVPO  Glandular kallikrein, prostatic (Tissue kallikrein) (
           esterase)
          Length = 239

 Score =  205 bits (522), Expect = 8e-52
 Identities = 94/235 (40%), Positives = 139/235 (59%), Gaps = 15/235 (6%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            V+ G   C +DSHP+QAA+Y     + CGGVL+DPQWVLTAAHC     + QV LG+HNL + E
Sbjct: 1   VIGGQECARDSHPWQAAVYYYSDIKCGGVLVDPQWVLTAAHCINDSNQVKLGRHNLFEDE 60

Query: 89  TFQRQISVDRTIVHPRYNP-----------ETHDNDIMMVHLKNPVKFSKKIQPLPLKND 137
              +    V +++ HP +N                E + +D+M++ L   P + +  +Q +PL
Sbjct: 61  DTAQHFLVSQSVPHPDFNMSLLEPHNVLPNEDYSHDLMLLRLNQPAQITDSVQVMPLPTQ 120

Query: 138 CSEENPNCQILGWGKMENGD----FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDM 193
              +     C+ LGWG ++         FPD +QC  + ++P + C+ A+     +T +M+CAGD+
Sbjct: 121 EVQVGTTCRALGWGSIDPDPAHPVFPDELQCVGLEILPSKNCDDAHIANVTGTMLCAGDL 180

Query: 194 KEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
              G D+C GDSGGPL+C G L+GL SWGD PCG     P +YT V  +   WI+   +
```

```
Sbjct: 181 AGGKDTCVGDSGGPLICDGVLQGLTSWGDSPCGVAHSPSLYTKVIEYREWIERTM 235
```

>gi|3318722|pdb|1AN1|E Chain E, Leech-Derived Tryptase InhibitorTRYPSIN COMPLEX
gi|9954879|pdb|1C9P|A Chain A, Complex Of Bdellastasin With Porcine Trypsin
Length = 223

```
 Score =  205 bits (522), Expect = 8e-52
 Identities = 94/222 (42%), Positives = 135/222 (60%), Gaps = 4/222 (1%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C  +S P+Q +L +  H  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1   IVGGYTCAANSIPYQVSLNSGSHF-CGGSLINSQWVVSAAHCYKSRIQVRLGEHNIDVLE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ I+  + I HP +N  T DNDIM++ L +P     ++  + L   C+     C I
Sbjct: 60  GNEQFINAAKIITHPNFNGNTLDNDIMLIKLSSPATLXSRVATVSLPRSCAAAGTECLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K     +P  +QC    ++    C+ +YPG+IT +M+C G ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGSSYPSLLQCLKAPVLSDSSCKSSYPGQITGNMICVGFLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG   C  K KPGVYT VC ++ WIQ  +
Sbjct: 180 PVVCNGQLQGIVSWG-YGCAQKNKPGVYTKVCNYVNWIQQTI 220
```

>gi|31541863|ref|NP_075822.2| RIKEN cDNA 2210010C04 [Mus musculus]
gi|12843046|dbj|BAB25837.1| unnamed protein product [Mus musculus]
Length = 247

```
 Score =  205 bits (521), Expect = 1e-51
 Identities = 99/246 (40%), Positives = 146/246 (59%), Gaps = 4/246 (1%)

Query: 5   MLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M T+  LA           ++ +K V G  C +++ P+Q +L  SG+  CGG LI+ QWV
Sbjct: 1   MKTLIFLAFLGAAVALPPDDDDDKNVGGYTCQRNALPYQVSL-NSGYHFCGGSLINSQWV 59

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
            ++AAHC K  +QV LG+HN+   E  ++ I   + I HP YN  T++NDIM++ LK
Sbjct: 60  VSAAHCYKSRIQVRLGEHNIDALEGGEQFIDAAKIIRHPNYNANTYNNDIMLIKLKTAAT 119

Query: 125 FSKKIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGK 182
             + ++  + L   C      C + GWG  + +G ++P  +QC D  ++    C  +YPGK
Sbjct: 120 LNSRVSTVALPRSCPSAGTRCLVSGWGNTLSSGTNYPSLLQCLDAPVLSDSSCTSSYPGK 179

Query: 183 ITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
            IT +M C G ++ G DSCQGDSGGP+VC G+L+G+VSWG   C  + KPGVYT VC ++
Sbjct: 180 ITSNMFCLGFLEGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAQRGKPGVYTKVCKYVN 238

Query: 243 WIQNIL 248
            WIQ  +
Sbjct: 239 WIQQTI 244
```

```
>gi|51593533|gb|AAH78492.1|  G  MGC85264 protein [Xenopus laevis]
          Length = 248

 Score =  205 bits (521), Expect = 1e-51
 Identities = 96/247 (38%), Positives = 150/247 (60%), Gaps = 5/247 (2%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M +  L  +    +A    + +K++ G  C    S P+Q  L  +G    CGG LI P+W+++A
Sbjct: 2    MPIWVLMFLAVAAAAPLDDDKIIGGYECTPHSQPWQVYLTQNGDRWCGGSLILPRWIISA 61

Query: 68   AHCKKPNLQVI--LGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKF 125
            AHC   P    ++   LG+H+L + ET ++ I V+    +H  YN +T+DNDIM+V L   P ++
Sbjct: 62   AHCYVPPETMVAHLGEHDLNKKETTEQHIQVESIYMHHGYNEDTYDNDIMLVKLVEPAQY 121

Query: 126  SKKIQPLPLKNDCSEENPNCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKI 183
            ++ +QP+P+    C +     C + G+G +          + D +QC D+ ++      C+ +YP KI
Sbjct: 122  NQYVQPIPVARSCPKAATECLVSGYGNLLAYGVKYADQLQCLDLPILSESSCKASYPKKI 181

Query: 184  TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
            +++M CAG ++ G DSCQGDSGGPL+C G L G+VSWG   C  K+ PGVY   VC ++ W
Sbjct: 182  SENMFCAGFLEGGKDSCQGDSGGPLICNGELYGVVSWG-WYCARKDLPGVYAKVCNYLDW 240

Query: 244  IQNILRN 250
            IQ+I  N
Sbjct: 241  IQDITNN 247


>gi|476488|pir||KQPG  tissue kallikrein (EC 3.4.21.35), pancreatic - pig  (tentative
           sequence)
          Length = 232

 Score =  205 bits (521), Expect = 1e-51
 Identities = 93/228 (40%), Positives = 137/228 (60%), Gaps = 8/228 (3%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            ++ G  C K+SHP+Q A+Y      CGGVL++P+WVLTAAHCK  N +V LG+HNL + E
Sbjct: 1    IIGGRECEKNSHPWQVAIYHYSSFQCGGVLVNPKWVLTAAHCKNDNYEVWLGRHNLFENE 60

Query: 89   TFQRQISVDRTIVHPRYN----PETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPN 144
               +    V      HP +N      + +D+M++ L++P  K +  ++ L L      E
Sbjct: 61   NTAQFFGVTADFPHPGFNLSADGKDYSHDLMLLRLQSPAKITDAVKVLELPTQEPELGST 120

Query: 145  CQILGWGKMENG----DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
            C+  GWG +E G    +FPD IQC  + L+    C  A+P K+T+SM+CAG +  G D+C
Sbjct: 121  CEASGWGSIEPGPDBFEFPDEIQCVQLTLLQNTFCABAHPBKVTESMLCAGYLPGGKDTC 180

Query: 201  QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGPL+C G  +G+ SWG  PCGS  KP +YT +  ++ WI + +
Sbjct: 181  MGDSGGPLICNGMWQGITSWGHTPCGSANKPSIYTKLIFYLDWINBTI 228


>gi|58257845|gb|AAW69364.1|  try13 [Macaca mulatta]
          Length = 247

 Score =  205 bits (521), Expect = 1e-51
 Identities = 98/233 (42%), Positives = 146/233 (62%), Gaps = 4/233 (1%)
```

```
Query: 18   AKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQV 77
            A +A  ++ +K+V G  C K+S P+Q +L  SG+  CGG LI+ QWV++A HC K  +QV
Sbjct: 13   AVAAPFDDDDKIVGGYTCGKNSLPYQVSL-NSGYHFCGGSLINNQWVVSAGHCYKTRIQV 71

Query: 78   ILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKND 137
             LG+HN+    E  ++ I+  + I HP YN  T +NDI+++ L +P   + ++   + L
Sbjct: 72   RLGEHNIEVLEGTEQFINAAKIIRHPNYNRNTLNNDILLIKLSSPAVINARVSTISLPTA 131

Query: 138  CSEENPNCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKE 195
                 C I GWG        D+PD +QC +   ++ + +CE +YPG+IT +M CAG ++
Sbjct: 132  PPAAGAKCLISGWGNTLSSGADYPDELQCLEAPVLTQAKCEASYPGRITSNMFCAGFLEG 191

Query: 196  GNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            G DSCQGDSGGP+V  G+L+G+VSWGD  C  K KPGVYT V  ++ WI+N +
Sbjct: 192  GKDSCQGDSGGPVVSNGQLQGIVSWGD-GCAQKNKPGVYTKVYNYLTWIKNTI 243
```

>gi|56606017|ref|NP_001008416.1| G kallikrein 1 [Bos taurus]
gi|33637117|gb|AAQ23715.1| G glandular kallikrein precursor [Bos taurus]
Length = 261

Score = 204 bits (519), Expect = 2e-51
Identities = 100/252 (39%), Positives = 146/252 (57%), Gaps = 16/252 (6%)

```
Query: 13   LCLVLAKSAWSEE---QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            LCL L+ +         Q ++V G  C K S P+Q A+Y      CGGVL+ PQWVLTAAH
Sbjct: 6    LCLALSLAGTGAVFPIQSRIVGGQECEKHSQPWQVAIYHFSTFQCGGVLVAPQWVLTAAH 65

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN-----------PETHDNDIMMVH 118
            CK  N QV LG+HNL + E    +    V      +P +N            E + +D+M++
Sbjct: 66   CKSDNYQVWLGRHNLFEDEDTAQFAGVSEDFPNPGFNLSLLENHTRHPGEDYSHDLMLLR 125

Query: 119  LKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCE 176
            L+ PV+ ++ +Q L L      +    C   GWG ++  +F  PD +QC D+ L+P E+C
Sbjct: 126  LQEPVQLTQNVQVLGLPTKEPQLGTTCYASGWGSVKPDEFSYPDDLQCVDLTLLPNEKCA 185

Query: 177  RAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTD 236
             A+P ++T+ M+CAG ++ G D+C GDSGGPL+C G L+G+ SWG +PCG+  KP VYT
Sbjct: 186  TAHPQEVTEWMLCAGHLEGGKDTCVGDSGGPLICEGMLQGITSWGHIPCGTPNKPSVYTK 245

Query: 237  VCTHIRWIQNIL 248
            V  ++ WI   +
Sbjct: 246  VILYLDWINKTM 257
```

>gi|20141454|sp|P00752|KLK_PIG Glandular kallikrein precursor (Tissue kallikrein)
Length = 246

Score = 204 bits (519), Expect = 2e-51
Identities = 94/238 (39%), Positives = 139/238 (58%), Gaps = 15/238 (6%)

```
Query: 26   QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
            Q +++ G  C K+SHP+Q A+Y      CGGVL++P+WVLTAAHCK  N +V LG+HNL
Sbjct: 5    QSRIIGGRECEKNSHPWQVAIYHYSSFQCGGVLVNPKWVLTAAHCKNDNYEVWLGRHNLF 64

Query: 86   QTETFQRQISVDRTIVHPRYN-----------PETHDNDIMMVHLKNPVKFSKKIQPLPL 134
            + E   +   V     HP +N            + + +D+M++ L++P K +  ++ L L
```

```
Sbjct: 65   ENENTAQFFGVTADFPHPGFNLSLLKXHTKADGKDYSHDLMLLRLQSPAKITDAVKVLEL 124

Query: 135  KNDCSEENPNCQILGWGKMENG----DFPDTIQCADVHLVPREQCERAYPGKITQSMVCA 190
                 E     C+   GWG +E G     +FPD IQC   + L+     C  A+P K+T+SM+CA
Sbjct: 125  PTQEPELGSTCEASGWGSIEPGPDBFEFPDEIQCVQLTLLQNTFCABAHPBKVTESMLCA 184

Query: 191  GDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            G +   G D+C GDSGGPL+C G  +G+ SWG   PCGS  KP +YT +  ++ WI + +
Sbjct: 185  GYLPGGKDTCMGDSGGPLICNGMWQGITSWGHTPCGSANKPSIYTKLIFYLDWINDTI 242
```

>gi|34856015|ref|XP_214932.2| G similar to GLANDULAR KALLIKREIN 8, PROSTATIC PRECUI
KALLIKREIN) (P1 KALLIKREIN) (RGK-8) [Rattus norvegicus]
Length = 261

```
 Score =  204 bits (518), Expect = 2e-51
 Identities = 99/259 (38%), Positives = 150/259 (57%), Gaps = 18/259 (6%)

Query: 8    MKMLALCLVLAKSAWSEE----QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQW 63
            M +L L L+L+   W++     Q +++ G  C K+S P+Q A+Y      CGGVLI P W
Sbjct: 1    MWLLILFLILSLG-WNDAAPPGQSRIIGGFNCEKNSQPWQVAVYHFNEPQCGGVLIHPSW 59

Query: 64   VLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPET-----------HDN 112
            V+TAAHC    N QV LG++NL + E F +   V ++   HP +N +              + N
Sbjct: 60   VITAAHCYSVNYQVWLGRNNLLEDEPFAQHRLVSQSFPHPGFNLDIIKNHTRKPGNDYSN 119

Query: 113  DIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLV 170
            D+M++HLK P    +  ++ + L  +  +    C    GWG +       +FPD +QC ++HL+
Sbjct: 120  DLMLLHLKTPADITDGVKVIDLPTEEPKVGSTCLTSGWGSITPLKWEFPDDLQCVNIHLL 179

Query: 171  PREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEK 230
              E+C +AY   ++T   M+CAG+M   G D C+GDSGGPL+C G L+G+ SWG MPCG   K
Sbjct: 180  SNEKCIKAYNDEVTDVMLCAGEMDGGKDICKGDSGGPLICDGVLQGITSWGSMPCGEPNK 239

Query: 231  PGVYTDVCTHIRWIQNILR 249
            P VYT +     WI+ +++
Sbjct: 240  PSVYTKLIKFTSWIKKVMK 258
```

>gi|27731319|ref|XP_218649.1| G similar to thymopsin [Rattus norvegicus]
Length = 249

```
 Score =  203 bits (516), Expect = 4e-51
 Identities = 98/249 (39%), Positives = 142/249 (57%), Gaps = 5/249 (2%)

Query: 3    MKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQ 62
            M +   + +L + L LA     + + E+++ G  C + SHP+Q AL      L CGGVL+
Sbjct: 1    MGVWLLSLLTVLLSLALET-AGQGERIIDGYKCKEGSHPWQVALLKGDQLHCGGVLVGES 59

Query: 63   WVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNP 122
            WVLTAAHCK      V LG   +        ++I     R+  HP Y+  TH NDIM+V +  P
Sbjct: 60   WVLTAAHCKMGQYTVHLGSDKIEDQSA--QRIKASRSFRHPGYSTRTHVNDIMLVKMDKP 117

Query: 123  VKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYP 180
            VK S K+Q + L + C        C + GWG    + D  FP  + C+DV L+  ++C++ Y
Sbjct: 118  VKMSDKVQKVKLPDHCEPPGTLCTVSGWGTTTSPDVTFPSDLMCSDVKLISSQECKKVYK 177
```

```
Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
             + ++M+CAG      ++C GDSGGPLVC   L+GLVSWG  PCG    PGVYT VC +
Sbjct: 178 DLLGKTMLCAGIPDSKTNTCNGDSGGPLVCNDTLQGLVSWGTYPCGQPNDPGVYTQVCKY 237

Query: 241 IRWIQNILR 249
            RW+++ ++
Sbjct: 238 QRWLEDTMK 246
```

>gi|56611173|gb|AAH87759.1| G Hypothetical LOC496640 [Xenopus tropicalis]
gi|58332122|ref|NP 001011209.1| G hypothetical LOC496640 [Xenopus tropicalis]
Length = 243

Score = 203 bits (516), Expect = 4e-51
Identities = 100/248 (40%), Positives = 158/248 (63%), Gaps = 8/248 (3%)

```
Query: 5   MLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
           M T+ + +L L LA +    E+ +K+V G  C   S P+Q +L   +G+  CGG LI+  WV
Sbjct: 1   MKTLLLFSL-LGLAVAQPIEDDDKIVGGYHC---SVPYQVSL-NAGYHFCGGSLINEHWV 55

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
           ++AAHC +  +++ +G++N+   E  ++ I   + I HP+YN  T DNDIM++ L+ P +
Sbjct: 56  VSAAHCYQSKMELRIGENNIELLEGTEQFIQSAKIIRHPQYNSWTIDNDIMLIQLQEPAQ 115

Query: 125 FSKKIQPLPLKNDCSEENPNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGK 182
            + ++QP+PL  +C       C I GWG  + NG ++PD +QC +  ++  ++C ++YPG
Sbjct: 116 LNNEVQPIPLPTECPPVGSICLISGWGNTLSNGVNYPDLLQCIEAPILSDQECRQSYPGS 175

Query: 183 ITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
           IT +M+C G ++ G DSCQGDSGGP+VC G L+G+VSWG   C     PGVYT VC ++
Sbjct: 176 ITDNMICVGYLEGGIDSCQGDSGGPVVCDGELQGVVSWG-RGCALPGYPGVYTKVCNYLS 234

Query: 243 WIQNILRN 250
           WI++ + N
Sbjct: 235 WIRDTIAN 242
```

>gi|54038747|gb|AAH84612.1| G LOC495211 protein [Xenopus laevis]
Length = 254

Score = 203 bits (516), Expect = 4e-51
Identities = 94/245 (38%), Positives = 148/245 (60%), Gaps = 3/245 (1%)

```
Query: 10  MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
           +L + ++L  +  ++  ++++ G  C+  S P+Q ALY     LCGG+LID  WVLTAAH
Sbjct: 2   LLLVAILLGSAVQTKTFDRIIGGEECVPHSQPWQVALYYFSDYLCGGILIDEWWVLTAAH 61

Query: 70  CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
           C + NLQV+LG HN  +    ++    +     ++P T++NDIM++ L +    +  +
Sbjct: 62  CNQSNLQVLLGAHNRTKPTDHKQYTYAVKICPRCDFDPVTYNNDIMLLKLASKANMNCHV 121

Query: 130 QPLPLKNDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYP-GKITQS 186
           + + L +D  E+N  C  GWG + + +  +PD +QC ++  V  +C+  YP  IT +
Sbjct: 122 KTIQLASDLVEDNTECLASGWGTITSPEENYPDKLQCVNLSTVSNSECQACYPEDDITDN 181

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
           M+CAG+M  G D+C+GDSGGPLVC G L G+ SWG  CG  KPGV+T V  +I WI +
```

```
Sbjct: 182 MLCAGNMAGGKDTCKGDSGGPLVCNGELHGITSWGHYICGLPNKPGVFTKVFNYIDWISD 241

Query: 247 ILRNK 251
           I++N+
Sbjct: 242 IMQNE 246


>gi|30584501|gb|AAP36503.1|  Homo sapiens kallikrein 5 [synthetic construct]
        Length = 294

 Score =  202 bits (515), Expect = 5e-51
 Identities = 94/230 (40%), Positives = 142/230 (61%), Gaps = 5/230 (2%)

Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTS-GHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKH 82
            +    ++++G  C    + P+QAAL        L CG VL+ PQW+LTAAHC+K    +V LG +
Sbjct: 62  DSSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHY 121

Query: 83  NLRQT-ETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEE 141
           +L     E+ Q+      ++I HP Y+    H ND+M++ L     ++ +K ++P+ + + C
Sbjct: 122 SLSPVYESGQQMFQGVKSIPHPGYSHPGHSNDLMLIKLNRRIRPTKDVRPINVSSHCPSA 181

Query: 142 NPNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDS 199
               C + GWG   K      FP   +QC ++ ++ +++CE AYP +I   +M CAGD K G DS
Sbjct: 182 GTKCLVSGWGTTKSPQVHFPKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGD-KAGRDS 240

Query: 200 CQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
           CQGDSGGP+VC G L+GLVSWGD PC     +PGVYT++C    +WIQ  ++
Sbjct: 241 CQGDSGGPVVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQ 290


>gi|37183138|gb|AAQ89369.1|  G  KLK5 [Homo sapiens]
 gi|31075483|gb|AAP42276.1|  G  kallikrein 5 splice variant 2 [Homo sapiens]
 gi|31075481|gb|AAP42275.1|  G  kallikrein 5 splice variant 1 [Homo sapiens]
 gi|30582573|gb|AAP35513.1|  G  kallikrein 5 [Homo sapiens]
 gi|6063033|gb|AAF03101.1|  G  stratum corneum tryptic enzyme [Homo sapiens]
 gi|6912644|ref|NP_036559.1|  G  kallikrein 5 preproprotein [Homo sapiens]
 gi|4589283|gb|AAD26429.1|  G  kallikrein-like protein 2 KLK-L2 [Homo sapiens]
 gi|14165478|gb|AAH08036.1|  G  Kallikrein 5, preproprotein [Homo sapiens]
 gi|9296994|sp|Q9Y337|KLK5_HUMAN  G  Kallikrein 5 precursor (Stratum corneum tryptic en
        (Kallikrein-like protein 2) (KLK-L2) (UNQ570/PRO1132)
        Length = 293

 Score =  202 bits (515), Expect = 5e-51
 Identities = 94/230 (40%), Positives = 142/230 (61%), Gaps = 5/230 (2%)

Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTS-GHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKH 82
            +    ++++G  C    + P+QAAL        L CG VL+ PQW+LTAAHC+K    +V LG +
Sbjct: 62  DSSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHY 121

Query: 83  NLRQT-ETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEE 141
           +L     E+ Q+      ++I HP Y+    H ND+M++ L     ++ +K ++P+ + + C
Sbjct: 122 SLSPVYESGQQMFQGVKSIPHPGYSHPGHSNDLMLIKLNRRIRPTKDVRPINVSSHCPSA 181

Query: 142 NPNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDS 199
               C + GWG   K      FP   +QC ++ ++ +++CE AYP +I   +M CAGD K G DS
```

```
Sbjct: 182 GTKCLVSGWGTTKSPQVHFPKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGD-KAGRDS 240

Query: 200 CQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
           CQGDSGGP+VC G L+GLVSWGD PC    +PGVYT++C   +WIQ  ++
Sbjct: 241 CQGDSGGPVVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQ 290


>gi|112403|pir||A34079  tissue kallikrein (EC 3.4.21.35) P1 precursor - rat
 gi|547791|sp|P36374|KLK8_RAT  G Prostatic glandular kallikrein 8 precursor (Tissue ka
          kallikrein) (RGK-8)
 gi|206640|gb|AAA42036.1|  kallikrein
          Length = 261

 Score =  202 bits (515), Expect = 5e-51
 Identities = 98/259 (37%), Positives = 150/259 (57%), Gaps = 18/259 (6%)

Query: 8   MKMLALCLVLAKSAWSEE----QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQW 63
           M +L L L+L+   W++     Q +++ G  C K+S P+Q A+Y      CGGVLI P W
Sbjct: 1   MWLLILFLILSLG-WNDAAPPGQSRIIGGFNCEKNSQPWQVAVYHFNEPQCGGVLIHPSW 59

Query: 64  VLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPET-----------HDN 112
           V+TAAHC   N QV LG++NL + E F +   V ++  HP +N +            + N
Sbjct: 60  VITAAHCYSVNYQVWLGRNNLLEDEPFAQHRLVSQSFPHPGFNLDIIKNHTRKPGNDYSN 119

Query: 113 DIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLV 170
           D+M++HLK P   +  ++ + L  +  +    C   GWG +     +FPD +QC ++HL+
Sbjct: 120 DLMLLHLKTPADITDGVKVIDLPTEEPKVGSTCLTSGWGSITPLKWEFPDDLQCVNIHLL 179

Query: 171 PREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEK 230
             E+C +AY  ++T  M+CAG+M  G D C+GDSGGPL+C G L+G+ SWG MPCG   K
Sbjct: 180 SNEKCIKAYNDEVTDVMLCAGEMDGGKDICKGDSGGPLICDGVLQGITSWGSMPCGEPNK 239

Query: 231 PGVYTDVCTHIRWIQNILR 249
           P VYT +     W++ +++
Sbjct: 240 PSVYTKLIKFTSWMKKVMK 258


>gi|21594212|gb|AAH32005.1|  G Stratum corneum chymotryptic enzyme, preproprotein [H
          Length = 253

 Score =  202 bits (515), Expect = 5e-51
 Identities = 95/247 (38%), Positives = 139/247 (56%), Gaps = 4/247 (1%)

Query: 5   MLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
           +L +++L L L L  +    + +K++ G PC + SHP+Q AL +   L CGGVL++ +WV
Sbjct: 6   LLPLQILLLSLALETAGEEAQGDKIIDGAPCARGSHPWQVALLSGNQLHCGGVLVNERWV 65

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
           LTAAHCK     V LG   L       ++I    ++  HP Y+ +TH ND+M+V L +  +
Sbjct: 66  LTAAHCKMNEYTVHLGSDTLGDRRA--QRIKASKSFRHPGYSTQTHVNDLMLVKLNSQAR 123

Query: 125 FSKKIQPLPLKNDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGK 182
            S  ++ + L + C      C + GWG   + D  FP  + C DV L+  + C + Y
Sbjct: 124 LSSMVKKVRLPSRCEPPGTTCTVSGWGTTTSPDVTFPSDLMCVDVKLISPQDCTKVYKDL 183

Query: 183 ITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
           +  SM+CAG      ++C GDSGGPLVC G L+GLVSWG  P G    PGVYT VC   +
```

```
Sbjct: 184 LENSMLCAGIPDSKKNACNGDSGGPLVCRGTLQGLVSWGTFPWGQPNDPGVYTQVCKFTK 243

Query: 243 WIQNILR 249
           WI + ++
Sbjct: 244 WINDTMK 250
```

>gi|41054557|ref|NP_955899.1| Unknown (protein for MGC:66382) [Danio rerio]
gi|33585756|gb|AAH55625.1| Unknown (protein for MGC:66382) [Danio rerio]
Length = 242

Score = 202 bits (515), Expect = 5e-51
Identities = 96/237 (40%), Positives = 147/237 (62%), Gaps = 3/237 (1%)

```
Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPN 74
           LVL  +A++ + +K+V G  C  +S P+QA+L  SG+  CGG L+   WV++AAHC K
Sbjct: 7   LVLLGAAFALDDDKIVGGYECQPNSQPWQASL-NSGYHFCGGSLVSEYWVVSAAHCYKSR 65

Query: 75  LQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           ++V LG+HN+   E  ++ I+ ++ I +P Y+    D+DIM++ L  P    +K +QP+ L
Sbjct: 66  VEVRLGEHNIVINEGTEQFITSEKVIRNPNYDSWDLDSDIMLIKLSKPATLNKYVQPVAL 125

Query: 135 KNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDM 193
            N C+ +   C++ GWG  M +    + +QC ++ ++    C  +YPG +T +M CAG +
Sbjct: 126 PNGCAADGTMCRVSGWGNTMSSTADSNKLQCLEIPILSDRDCNNSYPGMVTDTMFCAGYL 185

Query: 194 KEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
           + G DSCQGDSGGP+VC G L G+VSWG   C  K  PGVY  VC   +WI + +RN
Sbjct: 186 EGGKDSCQGDSGGPVVCNGELHGIVSWG-YGCAEKNHPGVYGKVCMFSQWIADTMRN 241
```

>gi|57162224|emb|CAI39655.1| OTTHUMP00000045395 [Homo sapiens]
gi|57160807|emb|CAI39514.1| OTTHUMP00000045395 [Homo sapiens]
Length = 247

Score = 202 bits (513), Expect = 9e-51
Identities = 94/227 (41%), Positives = 144/227 (63%), Gaps = 4/227 (1%)

```
Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
           ++ +K+V G  C ++S P+Q +L +  H  CGG LI  QWV++AAHC K  +QV LG+HN
Sbjct: 19  DDDDKIVGGYTCEENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHN 77

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
           ++  E  ++ I+  + I HP+YN +T DNDIM++ L +P   + ++   + L
Sbjct: 78  IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTTPPAAGT 137

Query: 144 NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
            C I GWG   +   D+PD ++C D  ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 138 ECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 197

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            DSGGP+VC G+L+G+VSWG   C  K +PGVYT V   ++ WI++ +
Sbjct: 198 RDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 243
```

>gi|55741639|ref|NP_001003262.1| kallikrein 1, renal/pancreas/salivary [Canis far

gi|631512|pir||S45303 tissue kallikrein (EC 3.4.21.35) precursor - dog
gi|414019|emb|CAA53210.1| kallikrein [Canis familiaris]
Length = 261

Score = 202 bits (513), Expect = 9e-51
Identities = 99/257 (38%), Positives = 146/257 (56%), Gaps = 16/257 (6%)

```
Query: 8   MKMLALCLVLAKS---AWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M  L LCL L+ +   A     Q +++ G  C K+S P+QAALY      CGGVL+ P+WV
Sbjct: 1   MWFLVLCLALSLAGTGAAPPVQSRIIGGWDCTKNSQPWQAALYHYSKFQCGGVLVHPEWV 60

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN-----------PETHDND 113
            +TAAHC    N Q+ LG++NL + E    + + V  +  HP +N             E + +D
Sbjct: 61  VTAAHCINDNYQLWLGRYNLFEHEDTAQFVQVRESFPHPEFNLSLLKNHTRLPEEDYSHD 120

Query: 114 IMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVP 171
            IM++ L  P + +  ++ L L      +    C   GWG +E    F  PD +QC D+ L+
Sbjct: 121 IMLLRLAEPAQITDAVRVLDLPTQEPQVGSTCYASGWGSIEPDKFIYPDDLQCVDLELLS 180

Query: 172 REQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKP 231
             + C  A+  K+T+ M+CAG ++ G D+C GDSGGPL+C G L+G+ SWG +PCGS    P
Sbjct: 181 NDICANAHSQKVTEFMLCAGHLEGGKDTCVGDSGGPLICDGVLQGITSWGHVPCGSPNMP 240

Query: 232 GVYTDVCTHIRWIQNIL 248
             VYT V +H+ WI+  +
Sbjct: 241 AVYTKVISHLEWIKETM 257
```

>gi|55662968|emb|CAH69873.1| protease, serine, 3 (mesotrypsin) [Homo sapiens]
gi|57162227|emb|CAI39658.1| protease, serine, 3 (mesotrypsin) [Homo sapiens]
gi|57160808|emb|CAI39515.1| protease, serine, 3 (mesotrypsin) [Homo sapiens]
Length = 304

Score = 202 bits (513), Expect = 9e-51
Identities = 94/227 (41%), Positives = 144/227 (63%), Gaps = 4/227 (1%)

```
Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L +  H  CGG LI  QWV++AAHC K  +QV LG+HN
Sbjct: 76  DDDDKIVGGYTCEENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHN 134

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            ++  E  ++ I+  + I HP+YN +T DNDIM++ L +P   + ++  + L
Sbjct: 135 IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTTPPAAGT 194

Query: 144 NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG    +   D+PD ++C D  ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 195 ECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 254

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             DSGGP+VC G+L+G+VSWG    C  K +PGVYT V  ++ WI++ +
Sbjct: 255 RDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 300
```

>gi|41350549|gb|AAS00515.1| trypsin [Oreochromis niloticus]
Length = 245

Score = 202 bits (513), Expect = 9e-51

```
 Identities = 96/242 (39%), Positives = 143/242 (59%), Gaps = 4/242 (1%)

Query: 11  LALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC 70
            + L L  A  A   E +K++ G  C K+S P+  +L   G+  CGG LI    W ++AAHC
Sbjct: 5   ILLALFAAAYAAPIEDDKIIGGYECAKNSVPYMVSL-NIGYHFCGGSLISSTWAVSAAHC 63

Query: 71  KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQ 130
             + ++Q+ LG+HN+    E  ++ IS  R I H  YN  T DNDIM++ L  P   +  ++
Sbjct: 64  YQSSIQLRLGEHNIAVNEGTEQFISSSRVIRHQSYNSYTLDNDIMLIKLSQPATLNSYVK 123

Query: 131 PLPLKNDCSEENPNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMV 188
             + L + C+     +C I GWG         ++PD + C +  ++     C  +YPG+IT +M
Sbjct: 124 TVSLPSGCAGAGTSCLISGWGNTSTSGSNYPDRLMCLNAPILSDTDCRNSYPGEITNNMF 183

Query: 189 CAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            CAG ++ G DSCQGDSGGP+VC G+L+G+VSWG   C   +++PGVYT VC +  WI N +
Sbjct: 184 CAGFLEGGKDSCQGDSGGPVVCNGQLQGIVSWG-YGCAQRDRPGVYTKVCNYNSWISNTM 242

Query: 249 RN 250
             N
Sbjct: 243 AN 244


>gi|55649803|ref|XP_524356.1|  G PREDICTED: similar to Kallikrein 15 precursor (ACO
            troglodytes]
           Length = 405

 Score =  201 bits (512), Expect = 1e-50
 Identities = 98/287 (34%), Positives = 151/287 (52%), Gaps = 60/287 (20%)

Query: 23  SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCK----------- 71
            +++ +K++ G  C   S P+Q ALY  G   CG  LI P WVL+AAHC+
Sbjct: 117 AQDGDKLLEGDECAPHSQPWQVALYERGRFNCGASLISPHWVLSAAHCQSRVLGKGNGVS 176

Query: 72  -----------------------------------KPN--LQVILGKHNLRQTETFQRQI 94
                                              +P+  ++V LG+HNLR+ +  ++
Sbjct: 177 RFLKGRGTSGCPLFDLSVLYLRVTTGPHSTGGKTTRPHSFMRVRLGEHNLRKRDGPEQLR 236

Query: 95  SVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKME 154
            +  R I HPRY   +H NDIM++ L  P + + +++P  L   C      C + GWG +
Sbjct: 237 TASRVIPHPRYEARSHRNDIMLLRLVQPARLTPQVRPAVLPTRCPHPGEACVVSGWGLVS 296

Query: 155 NGD------------FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQG 202
            + +              PDT+ CA++ ++    C+++YPG++T +MVCAG    G +SC+G
Sbjct: 297 HNEPGTAGSPRSQVSLPDTLHCANISIISDTSCDKSYPGRLTNTMVCAGAEGRGAESCEG 356

Query: 203 DSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
            DSGGPLVCGG L+G+VSWGD+PC +   KPGVYT VC ++ WI+  ++
Sbjct: 357 DSGGPLVCGGILQGIVSWGDVPCDNTTKPGVYTKVCHYLEWIRETMK 403


>gi|2564751|gb|AAC13322.1|  G  mesotrypsinogen [Homo sapiens]
 gi|47481110|gb|AAH69476.1|  G  Mesotrypsin, preproprotein [Homo sapiens]
 gi|47479560|gb|AAH69494.1|  G  Mesotrypsin, preproprotein [Homo sapiens]
 gi|21536452|ref|NP_002762.2|  G  mesotrypsin preproprotein [Homo sapiens]
 gi|1321640|dbj|BAA08257.1|  G  mesotrypsinogen [Homo sapiens]
```

```
         Length = 247

 Score =  201 bits (512), Expect = 1e-50
 Identities = 94/227 (41%), Positives = 144/227 (63%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C ++S P+Q +L +   H  CGG LI  QWV++AAHC K  +QV LG+HN
Sbjct: 19   DDDDKIVGGYTCEENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHN 77

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             ++  E  ++ I+  + I HP+YN +T DNDIM++ L +P   + ++   + L
Sbjct: 78   IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTAPPAAGT 137

Query: 144  NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG   +   D+PD ++C D  ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 138  ECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 197

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
              DSGGP+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 198  RDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 243
```

>gi|20988417|gb|AAH30238.1| G Unknown (protein for IMAGE:4537998) [Homo sapiens]

```
         Length = 251

 Score =  201 bits (512), Expect = 1e-50
 Identities = 94/227 (41%), Positives = 144/227 (63%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C ++S P+Q +L +   H  CGG LI  QWV++AAHC K  +QV LG+HN
Sbjct: 23   DDDDKIVGGYTCEENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHN 81

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             ++  E  ++ I+  + I HP+YN +T DNDIM++ L +P   + ++   + L
Sbjct: 82   IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTAPPAAGT 141

Query: 144  NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG   +   D+PD ++C D  ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 142  ECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 201

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
              DSGGP+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 202  RDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 247
```

>gi|1064991|pdb|1TRN|B S Chain B, Trypsin (E.C.3.4.21.4) Complexed With The Inhibit
Diisopropyl-Fluorophosphofluoridate (Dfp)
gi|1064990|pdb|1TRN|A S Chain A, Trypsin (E.C.3.4.21.4) Complexed With The Inhibitor
Diisopropyl-Fluorophosphofluoridate (Dfp)

```
         Length = 224

 Score =  201 bits (512), Expect = 1e-50
 Identities = 95/222 (42%), Positives = 142/222 (63%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++A HC K  +QV LG+HN+    E
Sbjct: 1    IVGGYNCEENSVPYQVSL-NSGYHFCGGSLINEQWVVSAGHCYKSRIQVRLGEHNIEVLE 59
```

```
Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ I+   + I HP+Y+  +T +NDIM++ L +     + ++   + L          C I
Sbjct: 60   GNEQFINAAKIIRHPQYDRKTLNNDIMLIKLSSRAVINARVSTISLPTAPPATGTKCLIS 119

Query: 149  GWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
             GWG    +     D+PD +QC D   ++ + +CE +YPGKIT +M C G ++ G DSCQGDSGG
Sbjct: 120  GWGNTASSGADYPDELQCLDAPVLSQAKCEASYPGKITSNMFCVGFLEGGKDSCQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             P+VC G+L+G+VSWGD  C  K KPGVYT V  +++WI+N +
Sbjct: 180  PVVCNGQLQGVVSWGD-GCAQKNKPGVYTKVYNYVKWIKNTI 220
```

>gi|6066378|emb|CAB58178.1| G trypsinogen IV a-form [Homo sapiens]
Length = 261

```
 Score =  201 bits (512), Expect = 1e-50
 Identities = 94/227 (41%), Positives = 144/227 (63%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C ++S P+Q +L +   H  CGG LI  QWV++AAHC K  +QV LG+HN
Sbjct: 33   DDDDKIVGGYTCEENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHN 91

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             ++  E  ++ I+  + I HP+YN +T DNDIM++ L +P   + ++  + L
Sbjct: 92   IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTAPPAAGT 151

Query: 144  NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG   +    D+PD ++C D   ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 152  ECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 211

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
              DSGGP+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 212  RDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 257
```

>gi|423134|pir||S33496 trypsin (EC 3.4.21.4) IV form a - human
gi|464951|sp|P35030|TRY3_HUMAN G Trypsin III precursor (Brain trypsinogen) (Mesotryp
(Trypsin IV)
Length = 304

```
 Score =  201 bits (512), Expect = 1e-50
 Identities = 94/227 (41%), Positives = 144/227 (63%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C ++S P+Q +L +   H  CGG LI  QWV++AAHC K  +QV LG+HN
Sbjct: 76   DDDDKIVGGYTCEENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHN 134

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             ++  E  ++ I+  + I HP+YN +T DNDIM++ L +P   + ++  + L
Sbjct: 135  IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTAPPAAGT 194

Query: 144  NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG   +    D+PD ++C D   ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 195  ECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 254
```

```
Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            DSGGP+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 255 RDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 300
```

>gi|30584977|gb|AAP36761.1| Homo sapiens kallikrein 2, prostatic [synthetic constru
        Length = 262

```
 Score =  201 bits (511), Expect = 2e-50
 Identities = 99/236 (41%), Positives = 136/236 (57%), Gaps = 13/236 (5%)

Query: 26  QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
            Q ++V G  C K S P+Q A+Y+ G   CGGVL+ PQWVLTAAHC K N QV LG+HNL
Sbjct: 22  QSRIVGGWECEKHSQPWQVAVYSHGWAHCGGVLVHPQWVLTAAHCLKKNSQVWLGRHNLF 81

Query: 86  QTETFQRQISVDRTIVHPRYN-----------PETHDNDIMMVHLKNPVKFSKKIQPLPL 134
            + E   +++ V  +  HP YN            E  +D+M++ L  P K +  ++ L L
Sbjct: 82  EPEDTGQRVPVSHSFPHPLYNMSLLKHQSLRPDEDSSHDLMLLRLSEPAKITDVVKVLGL 141

Query: 135 KNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQSMVCAGD 192
                    C   GWG +E  +F   P ++QC  +HL+  + C RAY  K+T+ M+CAG
Sbjct: 142 PTQEPALGTTCYASGWGSIEPEEFLRPRSLQCVSLHLLSNDMCARAYSEKVTEFMLCAGL 201

Query: 193 MKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
               G D+C GDSGGPLVC G L+G+ SWG  PC   EKP VYT V  + +WI++ +
Sbjct: 202 WTGGKDTCGGDSGGPLVCNGVLQGITSWGPEPCALPEKPAVYTKVVHYRKWIKDTI 257
```

>gi|30582139|gb|AAP35296.1| G kallikrein 2, prostatic [Homo sapiens]
gi|5031829|ref|NP_005542.1| G kallikrein 2, prostatic isoform 1 [Homo sapiens]
gi|13528792|gb|AAH05196.1| G Kallikrein 2, prostatic [Homo sapiens]
gi|6425046|gb|AAF08276.1| G prostrate kallikrein 2 [Homo sapiens]
gi|4261522|gb|AAD13816.1| G glandular kallikrein-1 [Homo sapiens]
gi|11244761|gb|AAG33356.1| G glandular kallikrein [Homo sapiens]
gi|88862|pir||A29586 tissue kallikrein (EC 3.4.21.35) hGK-1 precursor - human
gi|125174|sp|P20151|KLK2_HUMAN G Kallikrein 2 precursor (Tissue kallikrein 2) (Gland kallikrein-1) (hGK-1)
gi|386842|gb|AAA74454.1| G glandular kallikrein precursor
        Length = 261

```
 Score =  201 bits (511), Expect = 2e-50
 Identities = 99/236 (41%), Positives = 136/236 (57%), Gaps = 13/236 (5%)

Query: 26  QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
            Q ++V G  C K S P+Q A+Y+ G   CGGVL+ PQWVLTAAHC K N QV LG+HNL
Sbjct: 22  QSRIVGGWECEKHSQPWQVAVYSHGWAHCGGVLVHPQWVLTAAHCLKKNSQVWLGRHNLF 81

Query: 86  QTETFQRQISVDRTIVHPRYN-----------PETHDNDIMMVHLKNPVKFSKKIQPLPL 134
            + E   +++ V  +  HP YN            E  +D+M++ L  P K +  ++ L L
Sbjct: 82  EPEDTGQRVPVSHSFPHPLYNMSLLKHQSLRPDEDSSHDLMLLRLSEPAKITDVVKVLGL 141

Query: 135 KNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQSMVCAGD 192
                    C   GWG +E  +F   P ++QC  +HL+  + C RAY  K+T+ M+CAG
Sbjct: 142 PTQEPALGTTCYASGWGSIEPEEFLRPRSLQCVSLHLLSNDMCARAYSEKVTEFMLCAGL 201
```

```
Query: 193 MKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             G D+C GDSGGPLVC G L+G+ SWG  PC   EKP VYT V  + +WI++ +
Sbjct: 202 WTGGKDTCGGDSGGPLVCNGVLQGITSWGPEPCALPEKPAVYTKVVHYRKWIKDTI 257
```

>gi|422723|pir||S33772 tissue kallikrein (EC 3.4.21.35) precursor, renal - crab-eat macaque
gi|585360|sp|Q07276|KLK1_MACFA Kallikrein 1 precursor (Tissue kallikrein) (Kidney/pancreas/salivary gland kallikrein)
gi|293141|gb|AAA36853.1| pre-pro-protein for kallikrein
Length = 257

Score = 201 bits (511), Expect = 2e-50
Identities = 98/256 (38%), Positives = 146/256 (57%), Gaps = 18/256 (7%)

```
Query: 8   MKMLALCLVLAKSAWSEE---QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M  L LCL L+            Q ++V G  C   S P+QAALY       CGG+L+ PQWV
Sbjct: 1   MWFLVLCLALSLGGTGRAPPIQSRIVGGWEC---SQPWQAALYHFSTFQCGGILVHPQWV 57

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN----------PETHDNDI 114
            LTAAHC    N Q+ LG+HNL    E    + + V   +  HP +N             + + +D+
Sbjct: 58  LTAAHCISDNYQLWLGRHNLFDDEDTAQFVHVSESFPHPGFNMSLLKNHTRQADDYSHDL 117

Query: 115 MMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLVPR 172
            M++ L   P + +  +Q + L      E     C    GWG +E  N   FPD +QC D+ ++P
Sbjct: 118 MLLRLTQPAEITDAVQVVELPTQEPEVGSTCLASGWGSIEPENFSFPDDLQCVDLEILPN 177

Query: 173 EQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPG 232
            ++C +A+   K+T+  M+CAG ++ G D+C GDSGGPL C G L+G+ SWG +PCGS   KP
Sbjct: 178 DECAKAHTQKVTEFMLCAGHLEGGKDTCVGDSGGPLTCDGVLQGVTSWGYIPCGSPNKPA 237

Query: 233 VYTDVCTHIRWIQNIL 248
            V+  V ++++WI++ +
Sbjct: 238 VFVKVLSYVKWIEDTI 253
```

>gi|46402490|ref|NP_571783.1| trypsin [Danio rerio]
gi|27464842|gb|AAO16212.1| trypsin precursor [Danio rerio]
Length = 243

Score = 201 bits (511), Expect = 2e-50
Identities = 95/232 (40%), Positives = 142/232 (61%), Gaps = 4/232 (1%)

```
Query: 10  MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            +LAL  V    +    ++ +K+V G  C K+  P+Q +L  SG+  CGG LI   WV++AAH
Sbjct: 6   LLALFAVAYAAPLGDDDDKIVGGYECTKNGVPYQVSL-NSGYHFCGGSLISNLWVVSAAH 64

Query: 70  CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C K  +QV LG+HN+  TE  ++ I+ ++ I HP YN  T DND+M++ L +  + +  +
Sbjct: 65  CYKSRVQVRLGEHNIDVTEGTEQFINSEKVIRHPSYNSNTLDNDVMLIKLSSSAQINSYV 124

Query: 130 QPLPLKNDCSEENPNCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 187
            + + L + C+    +C I GWG M     ++P  + C +  ++   C AYPG+I+ +M
Sbjct: 125 KTVSLPSSCASSGTSCLISGWGNMSASGSNYPSRLMCLNAPILSDSTCRNAYPGQISSNM 184

Query: 188 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCT 239
             CAG M+ G DSCQGDSGGP+VC  +L+G+VSWG  C  + KPGVY  VCT
```

```
Sbjct: 185  FCAGFMEGGKDSCQGDSGGPVVCNNQLQGIVSWG-YGCAQRNKPGVYAKVCT 235


>gi|58257846|gb|AAW69365.1|   try12 [Macaca mulatta]
          Length = 247

 Score =  201 bits (511), Expect = 2e-50
 Identities = 93/227 (40%), Positives = 142/227 (62%), Gaps = 4/227 (1%)

Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C ++S P+Q +L  SG+  CGG LI  QWV++A HC KP+++V LG+HN
Sbjct: 19   DDDDKIVGGNTCEENSVPYQVSL-NSGYHFCGGSLISEQWVVSAGHCYKPHIEVRLGEHN 77

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +   E  ++ I+  + I H +YN  T +NDIM++ L  P   +  + +PL N
Sbjct: 78   IEVLEGNEQFINATKIIRHSKYNGNTLNNDIMLIKLSTPAVINDYVSTIPLPNAPPAAGT 137

Query: 144  NCQILGWGK--MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG       D+PD +QC D  ++ + +C+ +YP +IT +M C G ++ G DSCQ
Sbjct: 138  ECLISGWGNTLSSGADYPDELQCLDAPVLTQTKCKLSYPFRITSNMFCVGFLEGGKDSCQ 197

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG    C   K +PGVYT V   ++ WI++ +
Sbjct: 198  GDSGGPVVCNGQLQGIVSWG-YGCALKRRPGVYTKVYNYVDWIKDTI 243


>gi|41350551|gb|AAS00516.1|   trypsin [Oreochromis aureus]
          Length = 245

 Score =  201 bits (511), Expect = 2e-50
 Identities = 96/242 (39%), Positives = 142/242 (58%), Gaps = 4/242 (1%)

Query: 11   LALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC 70
             + L L  A  A   E +K++ G  C K+S P+  +L   G+  CGG LI   W ++AAHC
Sbjct: 5    ILLALFAAAYAAPIEDDKIIGGYECAKNSVPYMVSL-NIGYHFCGGSLISSTWAVSAAHC 63

Query: 71   KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQ 130
              + ++Q+ LG+HN+   E  ++ IS  R I H  YN  T DNDIM++ L  P   +  ++
Sbjct: 64   YQSSIQLRLGEHNIAVNEGTEQFISSSRVIRHQSYNSYTLDNDIMLIKLSQPATLNSYVK 123

Query: 131  PLPLKNDCSEENPNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMV 188
              + L + C+    +C I GWG        ++PD + C +  ++     C  +YPG+IT +M
Sbjct: 124  TVSLPSGCAGAGTSCLISGWGNTSTSGSNYPDRLMCLNAPILSDTDCRNSYPGEITNNMF 183

Query: 189  CAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             CAG ++ G DSCQGDSGGP+VC G+L+G+VSWG   C  + +PGVYT VC +  WI N +
Sbjct: 184  CAGFLEGGKDSCQGDSGGPVVCNGQLQGIVSWG-YGCAQRNRPGVYTKVCNYNSWISNTM 242

Query: 249  RN 250
              N
Sbjct: 243  AN 244


>gi|27573671|pdb|1J17|T  Chain T, Factor Xa Specific Inhibitor In Complex With Rat
          Mutant X99175190RT
 gi|27573670|pdb|1J16|A  Chain A, Benzamidine In Complex With Rat Trypsin Mutant X99
```

```
gi|27573669|pdb|1J15|A  Chain A, Benzamidine In Complex With Rat Trypsin Mutant X99
         Length = 223

 Score =  201 bits (511), Expect = 2e-50
 Identities = 95/222 (42%), Positives = 144/222 (64%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+HN+   E
Sbjct: 1    IVGGYTCQENSVPYQVSL-NSGYHFCGGSLINDQWVVSAAHCYKSRIQVRLGEHNINVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
               ++ ++  + I HP ++ ET++NDIM++ L +PVK + ++  + L + C+     C I
Sbjct: 60   GNEQFVNAAKIIKHPNFDRETYNNDIMLIKLSSPVKLNARVATVALPSSCAPAGTQCLIS 119

Query: 149  GWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
             GWG  + +G + PD +QC D  L+P+  CE +    IT +MVC G ++ G D+CQGDSGG
Sbjct: 120  GWGNTLSSGVNEPDLLQCLDAPLLPQADCEASSSFIITDNMVCVGFLEGGKDACQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             P+VC G L+G+VSWG   C    + PGVYT VC ++ WIQ+ +
Sbjct: 180  PVVCNGELQGIVSWG-YGCALPDNPGVYTKVCNYVDWIQDTI 220


 >gi|5441853|dbj|BAA82362.1|   trypsinogen 1 [Paralichthys olivaceus]
         Length = 242

 Score =  201 bits (511), Expect = 2e-50
 Identities = 96/242 (39%), Positives = 148/242 (61%), Gaps = 4/242 (1%)

Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
             M+ L   L++  +A++ E +K+V G  C   S P Q +L  SG+  CGG L++  WV++A
Sbjct: 1    MRSLVFVLLIG-AAFAMEDDKIVGGYECTPYSQPHQVSL-NSGYHFCGGSLVNENWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
             AHC K  ++V +G+H+++  E   ++ IS +R I HP Y+    +NDIM++ L+ P   ++
Sbjct: 59   AHCYKSRVEVRMGEHHIKINEGTEQFISSERVIRHPNYSSYNINNDIMLIKLREPATLNQ 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQS 186
              +QP+ L   C+     C + GWG  M +   D +QC D+ ++    CE +YPG IT +
Sbjct: 119  YVQPVALPTSCAPAGTMCTVSGWGNTMSSTANRDMLQCLDLPILSDRDCENSYPGMITPA 178

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
             M CAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C   ++ PGVY  VC  I W++
Sbjct: 179  MFCAGYLEGGKDSCQGDSGGPVVCNGELQGVVSWG-YGCAERDHPGVYARVCIFIDWLET 237

Query: 247  IL 248
              +
Sbjct: 238  TM 239


 >gi|9665236|ref|NP_062544.1|  kallikrein 12 isoform 1 [Homo sapiens]
 gi|6249632|gb|AAF06065.1|  kallikrein-like protein 5-related protein 1 [Homo sapien
 gi|10799397|gb|AAG23258.1|  kallikrein 12 [Homo sapiens]
         Length = 254

 Score =  201 bits (510), Expect = 2e-50
```

```
 Identities = 102/238 (42%), Positives = 145/238 (60%), Gaps = 10/238 (4%)

Query: 6   LTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVL 65
           L++ +L   L L+++A       K+ +G  C ++S P+Q  L+     L CGGVLID +WVL
Sbjct: 3   LSIFLLLCVLGLSQAA----TPKIFNGTECGRNSQPWQVGLFEGTSLRCGGVLIDHRWVL 58

Query: 66  TAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRY--NPETHDNDIMMVHLKNPV 123
           TAAHC        V LG+H+L Q +   ++          ++ HP Y     +H++D+ ++ L+ PV
Sbjct: 59  TAAHCSGSRYWVRLGEHSLSQLDWTEQIRHSGFSVTHPGYLGASTSHEHDLRLLRLRLPV 118

Query: 124 KFSKKIQPLPLKNDCSEENPNCQILGWG--KMENGDFPDTIQCADVHLVPREQCERAYPG 181
           + +   +QPLPL NDC+        C + GWG            FPD +QC ++ +V      C      YPG
Sbjct: 119 RVTSSVQPLPLPNDCATAGTECHVSGWGITNHPRNPFPDLLQCLNLSIVSHATCHGVYPG 178

Query: 182 KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDM-PCGSKEKPGVYTDVC 238
           +IT +MVCAG +  G D+CQGDSGGPLVCGG L+GLVSWG + PCG     PGVYT +C
Sbjct: 179 RITSNMVCAGGV-PGQDACQGDSGGPLVCGGVLQGLVSWGSVGPCGQDGIPGVYTYIC 235
```

>gi|52345790|ref|NP_001004941.1| G MGC89184 protein [Xenopus tropicalis]
gi|49670651|gb|AAH75423.1| G MGC89184 protein [Xenopus tropicalis]
Length = 249

```
 Score =  200 bits (508), Expect = 3e-50
 Identities = 96/244 (39%), Positives = 143/244 (58%), Gaps = 6/244 (2%)

Query: 12  ALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCK 71
           A+  +   +A   +  ++V G  C   S P+Q  L   G   CGG LI P+W+++AAHC
Sbjct: 6   AMMFLAVAAAGPLDDSRIVGGYECAPHSKPWQVHLNYKGSFFCGGSLIAPRWIVSAAHCY 65

Query: 72  KPNLQVI--LGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
               V+  +G H++  + E   + I V+++  H +YN    DNDIM++ L  P +F+   +
Sbjct: 66  LLPKYVVAHIGMHDVSKAEGTVQIIQVEKSFQHYKYNSSNIDNDIMLIKLAEPAQFNHHV 125

Query: 130 QPLPLKNDCSEENPNCQILGWGKMENG---DFPDTIQCADVHLVPREQCERAYPGKITQS 186
           QP+PL + C   +    C + G+G M  G    +FPD +QC D+ ++P + C+ +Y   IT +
Sbjct: 126 QPIPLAHSCPMKGTRCVVSGYGNMRPGFFGEFPDRLQCLDLPVLPEDSCKSSYGDDITNN 185

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
           M CAG  + G DSCQGDSGGPLVC G L G+VSWG   C  K  PGVYT VC +I W+ +
Sbjct: 186 MFCAGFQEGGKDSCQGDSGGPLVCDGELFGVVSWGH-ECAKKGYPGVYTKVCHYIDWVND 244

Query: 247 ILRN 250
           I+ +
Sbjct: 245 IMED 248
```

>gi|13516891|dbj|BAB40329.1| trypsinogen [Engraulis japonicus]
Length = 240

```
 Score =  200 bits (508), Expect = 3e-50
 Identities = 93/234 (39%), Positives = 142/234 (60%), Gaps = 3/234 (1%)

Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPN 74
           LVL  +A++E+ +K+V G  C   S P   +L  SG+  CGG L++  WV++AAHC K
Sbjct: 7   LVLLGAAFAED-DKIVGGYECQAHSQPHTVSL-NSGYHFCGGSLVNENWVVSAAHCYKSR 64
```

```
Query: 75  LQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           ++V LG+H++ Q E  ++ I   R I HP+Y+    DND+M++ L  P   ++ +QP+ L
Sbjct: 65  VEVRLGEHHIGQNENTEQFIDSSRVIRHPQYSSYNIDNDVMLIKLSTPATLNQYVQPVAL 124

Query: 135 KNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMK 194
            + C+      C + GWG    +     D +QC  + ++     C+ +YPG IT +M CAG ++
Sbjct: 125 PSRCASAGTMCLVAGWGNTMSNVSGDKLQCLQIPILSDRDCDNSYPGMITDAMFCAGYLE 184

Query: 195 EGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            G DSCQGDSGGP+VC G L+G+VSWG    C   ++ PGVY  VC    W+Q+ +
Sbjct: 185 GGKDSCQGDSGGPVVCNGELQGVVSWG-YGCAERDHPGVYAKVCIFTDWLQSTM 237
```

>gi|230765|pdb|2TLD|E Chain E, Bovine Trypsin (E.C.3.4.21.4) Complex With A Modii
(Streptomyces Subtilisin Inhibitor) With Met 70 Replaced
By Gly And Met 73 Replaced By Lys (SSI(M70G,M73K))
Length = 220

Score = 200 bits (508), Expect = 3e-50
Identities = 97/222 (43%), Positives = 139/222 (62%), Gaps = 7/222 (3%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
           +V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1   IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
             ++ IS  ++IVHP YN  T +NDIM++ LK+    + ++  + L   C+     C I
Sbjct: 60  GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
           GWG  K      +PD ++C     ++    C+ AYPG+IT +M CAG    EG DSCQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSAYPGQITSNMFCAG--LEGGDSCQGDSGG 177

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           P+VC G+L+G+VSWG   C +K KPGVYT VC ++ WI+  +
Sbjct: 178 PVVCSGKLQGIVSWGS-GC-AKNKPGVYTKVCNYVSWIKQTI 217
```

>gi|29366812|ref|NP_036447.1| kallikrein 9 [Homo sapiens]
gi|5919239|gb|AAD26427.2| kallikrein-like protein 3 [Homo sapiens]
gi|11244767|gb|AAG33362.1| kallikrein-like 3 [Homo sapiens]
gi|10799394|gb|AAG23255.1| kallikrein 9 [Homo sapiens]
gi|9296988|sp|Q9UKQ9|KLK9_HUMAN Kallikrein 9 precursor (Kallikrein-like protein 3)
Length = 250

Score = 199 bits (507), Expect = 4e-50
Identities = 101/247 (40%), Positives = 142/247 (57%), Gaps = 8/247 (3%)

```
Query: 10  MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
           + AL  +LA   W++    + +     C  +S P+QA L+     L CG  LI   +W+LTAAH
Sbjct: 6   LCALLSLLAGHGWADT--RAIGAEECRPNSQPWQAGLFHLTRLFCGATLISDRWLLTAAH 63

Query: 70  CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPET----HDNDIMMVHLKNPVKF 125
           C+KP L V LG+H+L + E  ++   V     HP +N +     H++DIM++ L     +
Sbjct: 64  CRKPYLWVRLGEHHLWKWEGPEQLFRVTDFFPHPGFNKDLSANDHNDDIMLIRLPRQARL 123
```

```
Query: 126 SKKIQPLPLKNDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGKI 183
           S  +QPL L   C        C I GWG + +    FP T+QCA++ ++    + C  AYPG I
Sbjct: 124 SPAVQPLNLSQTCVSPGMQCLISGWGAVSSPKALFPVTLQCANISILENKLCHWAYPGHI 183

Query: 184 TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
           + SM+CAG   + G   SCQGDSGGPLVC G L G+VS G   PC     +P VYT VC ++ W
Sbjct: 184 SDSMLCAGLWEGGRGSCQGDSGGPLVCNGTLAGVVSGGAEPCSRPRRPAVYTSVCHYLDW 243

Query: 244 IQNILRN 250
           IQ I+ N
Sbjct: 244 IQEIMEN 250
```

>gi|57113723|ref|XP_537938.1| PREDICTED: similar to KLK15 [Canis familiaris]
Length = 643

Score = 199 bits (507), Expect = 4e-50
Identities = 88/227 (38%), Positives = 138/227 (60%), Gaps = 12/227 (5%)

```
Query: 39  SHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDR 98
           S  +Q AL+  G   CG  LI    WVL+AAHC+    ++   LG+HNLR+ +   ++   ++ R
Sbjct: 397 SPTWQVALFERGRFNCGASLISEHWVLSAAHCQTRFMRARLGEHNLRKRDGPEQLRTLAR 456

Query: 99  TIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENG-- 156
            I HP Y   +H +D+M++ L  P + S++++P+ L   C +    C + GWG + +
Sbjct: 457 IIPHPLYEAHSHRHDVMLLRLTRPARLSRQVRPVALPTRCPQPAEACVVSGWGLVSDHKP 516

Query: 157 ----------DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
                       PDT+ CA++ ++P    C + YPG++  SM+CAG    G +SC+GDSGG
Sbjct: 517 GTKGSTDSQVSLPDTLHCANISVIPAASCNKDYPGRLVASMLCAGAEGGGTESCEGDSGG 576

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRNKWL 253
           PLVC G L+G+VSWGD+PC +   KPGVYT VC+++ WI+  ++   +L
Sbjct: 577 PLVCRGVLQGIVSWGDVPCDTTTKPGVYTKVCSYLEWIKETMKRNYL 623
```

Score = 87.0 bits (214), Expect = 4e-16
Identities = 53/192 (27%), Positives = 80/192 (41%), Gaps = 50/192 (26%)

```
Query: 40  HPFQAALYTSGHLLCGGVLIDPQWVLTAAHC---------------------------- 70
           HP QAALY       CGGVL+ P+WVLTAAHC
Sbjct: 25  HPLQAALYHYSKFQCGGVLVHPEWVLTAAHCINSKWGQGIADDGDGSERDPQRTGRDYPD 84

Query: 71  --------KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN-----------PETHD 111
                    + N Q+ LG++NL + E   + + +  +  HP +N            E +
Sbjct: 85  MCVYDKDALQGNYQLWLGRYNLFEHEDTAQLVQIRESFPHPEFNLSFLKNHTRLPEEDYS 144

Query: 112 NDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHL 169
           +D+M++ L   P + +  ++ L L      +    C   GWG +E    F  PD +QC D+ L
Sbjct: 145 HDLMLLRLAEPTQITDAVRVLDLPTQEPQVGSTCCASGWGCIEPDKFIYPDDLQCVDLQL 204

Query: 170 VPREQCERAYPG 181
           +  + C   Y G
Sbjct: 205 LSNDVCGNTYTG 216
```

>gi|32402373|gb|AAP81159.1| trypsinogen [Pangasius hypophthalmus]
Length = 242

Score = 199 bits (507), Expect = 4e-50
Identities = 104/245 (42%), Positives = 145/245 (59%), Gaps = 5/245 (2%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
             M+ L L L+L  + ++ E +K+V G  C   S P+Q +L    H  CGG LI+  WV++A
Sbjct: 1    MRSLVL-LLLVGACFALEDDKIVGGYECTPYSQPWQVSLNVGYHF-CGGSLINQNWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
             AHC +  ++V LG+HN++  E  ++ IS  R I HP YN  T DNDIM++ L      +
Sbjct: 59   AHCYQSRIEVRLGEHNIQINEGTEQFISSSRVIRHPNYNSWTIDNDIMLIKLSQSASVNN 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQS 186
              +QP+ L + C      C + GWG  M +    + +QC +V ++  E C  +YPG IT++
Sbjct: 119  YVQPVALPSSCPPAGTWCIVSGWGNTMSSTADRNKLQCVEVPILSDEDCNNSYPGMITKA 178

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWI-Q 245
             M CAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C  K  PGVYT VC    WI Q
Sbjct: 179  MFCAGFLEGGKDSCQGDSGGPVVCNGELQGIVSWG-YGCAEKNHPGVYTKVCIFTDWIAQ 237

Query: 246  NILRN 250
              I  N
Sbjct: 238  TIASN 242
```

>gi|34856017|ref|XP_214931.2| G similar to kallikrein [Rattus norvegicus]
Length = 410

Score = 199 bits (506), Expect = 6e-50
Identities = 94/236 (39%), Positives = 142/236 (60%), Gaps = 17/236 (7%)

```
Query: 26   QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
             Q +VV G  C K+S P+Q A+      LCGGVLIDP WV+TAAHC   N  V+LG++NL
Sbjct: 177  QSRVVGGFKCEKNSQPWQVAVINED--LCGGVLIDPSWVITAAHCYSDNYHVLLGQNNL- 233

Query: 86   QTETFQRQISVDRTIVHPRYNP----------ETHDNDIMMVHLKNPVKFSKKIQPLPLK 135
              +E  Q ++ V ++  HP Y P          + + ND+M++HL  P   +  ++ + L
Sbjct: 234  -SEDVQHRL-VSQSFRHPDYKPFLMRNHTRKPKDYSNDLMLLHLSEPADITDGVKVIDLP 291

Query: 136  NDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDM 193
                 +    C + GWG     +  FPD +QC ++HL+  E+C +AY  K+T  M+CAG++
Sbjct: 292  TKEPKVGSTCLVSGWGSTNPSEWEFPDDLQCVNIHLLSNEKCIKAYKEKVTDLMLCAGEL 351

Query: 194  KEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
             + G D+C+GDSGGPL+C G L+G+ SWG +PCG   KPG+YT +     WI+ +++
Sbjct: 352  EGGKDTCRGDSGGPLICDGVLQGITSWGSVPCGEPNKPGIYTKLIKFTSWIKEVMK 407
```

>gi|559508|emb|CAA57701.1| trypsin [Paranotothenia magellanica]
gi|1086279|pir||S49489 trypsin (EC 3.4.21.4) precursor - Paranotothenia magellanica
Length = 242

Score = 199 bits (506), Expect = 6e-50
Identities = 94/244 (38%), Positives = 148/244 (60%), Gaps = 4/244 (1%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M+ L    L++   +A++ E++K+V G   C    S P Q +L  SG+   CGG L++   WV++A
Sbjct: 1    MRSLVFVLLIG-AAFATEEDKIVGGKECSPYSQPHQVSL-NSGYHFCGGSLVNENWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K   ++V  +G+H++R TE    ++ IS   R I HP Y+     DNDIM++ L   P    ++
Sbjct: 59   AHCYKSRVEVRMGEHHIRVTEGKEQFISSSRVIRHPNYSSYNIDNDIMLIKLSKPATLNQ 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGKMENGDFP-DTIQCADVHLVPREQCERAYPGKITQS 186
             +Q  + L  + C+       C + GWG  ++        + +QC ++ ++        C+ +YPG IT +
Sbjct: 119  YVQAVALPSSCAPAGTMCTVSGWGSTQSSSADGNKLQCLNIPILSDRDCDNSYPGMITDA 178

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M CAG ++ G DSCQGDSGGP+VC G L+G+VSWG    C   ++ PGVY   VC     W++
Sbjct: 179  MFCAGYLQGGKDSCQGDSGGPVVCNGELQGVVSWG-YGCAERDHPGVYAKVCLFNDWLET 237

Query: 247  ILRN 250
             + N
Sbjct: 238  SMAN 241
```

>gi|49259459|pdb|1V2M|T S Chain T, Benzamidine In Complex With Bovine Trypsin Varia
X(Triple.Glu)bt.A1
gi|49259458|pdb|1V2L|T S Chain T, Benzamidine In Complex With Bovine Trypsin Variant
X(Triple.Glu)bt.D1
gi|49259457|pdb|1V2K|T S Chain T, Factor Xa Specific Inhibitor In Complex With Bovin
Trypsin Variant X(Triple.Glu)bt.D2
Length = 223

Score = 199 bits (506), Expect = 6e-50
Identities = 93/222 (41%), Positives = 138/222 (62%), Gaps = 4/222 (1%)

```
Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C   ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1    IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ IS  ++IVHP YN ET++NDIM++ LK+     + ++  + L    C+     C I
Sbjct: 60   GNEQFISASKSIVHPSYNSETYNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149  GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K       +PD ++C     ++     C+ A      IT +M CAG ++ G D+CQGDSGG
Sbjct: 120  GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSASSFIITSNMFCAGYLEGGKDACQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG+  C  K KPGVYT VC ++ WI+ +
Sbjct: 180  PVVCSGKLQGIVSWGE-GCAQKNKPGVYTKVCNYVSWIKQTI 220
```

>gi|609585|gb|AAA58782.1| G kallikrein
Length = 239

Score = 199 bits (506), Expect = 6e-50
Identities = 94/236 (39%), Positives = 142/236 (60%), Gaps = 17/236 (7%)

```
Query: 26   QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
            Q +VV G  C K+S P+Q A+      LCGGVLIDP WV+TAAHC   N  V+LG++NL
```

```
Sbjct: 6    QSRVVGGFKCEKNSQPWQVAVINED--LCGGVLIDPSWVITAAHCYSDNYHVLLGQNNL- 62

Query: 86   QTETFQRQISVDRTIVHPRYNP----------ETHDNDIMMVHLKNPVKFSKKIQPLPLK 135
             +E  Q ++ V ++  HP Y P          + + ND+M++HL  P   +  ++ + P
Sbjct: 63   -SEDVQHRL-VSQSFRHPDYKPFLMRNHTRKPKDYSNDLMLLHLSEPADITDGVKVIDLP 120

Query: 136  NDCSEENPNCQILGWGKMENGD--FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDM 193
                 +     C + GWG      +  FPD +QC ++HL+  E+C +AY  K+T  M+CAG++
Sbjct: 121  TKEPKVGSTCLVSGWGSTNPSEWEFPDDLQCVNIHLLSNEKCIKAYKEKVTDLMLCAGEL 180

Query: 194  KEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
             + G D+C+GDSGGPL+C G L+G+ SWG +PCG   KPG+YT +      WI+ +++
Sbjct: 181  EGGKDTCRGDSGGPLICDGVLQGITSWGSVPCGEPNKPGIYTKLIKFTSWIKEVMK 236
```

>gi|1552516|gb|AAC80208.1| trypsinogen C [Homo sapiens]
Length = 247

Score = 198 bits (504), Expect = 1e-49
Identities = 93/227 (40%), Positives = 139/227 (61%), Gaps = 4/227 (1%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
             ++ +K+V G  C ++S P+Q +L +  H  CGG LI  QWV++A HC KP++QV LG+HN
Sbjct: 19   DDDDKIVGGYTCEENSVPYQVSLNSGSHF-CGGSLISEQWVVSAGHCYKPHIQVRLGEHN 77

Query: 84   LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
             +    E  ++ I+  + I HP+YN  T +NDIM++ L  P    +  + L
Sbjct: 78   IEVLEGNEQFINAAKIIRHPKYNRITLNNDIMLIKLSTPAVINAHVSTISLPTAPPAAGT 137

Query: 144  NCQILGWGK--MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
              C I GWG        D+PD +QC D  ++ + +C+ +YP KIT  M C G ++ G DSCQ
Sbjct: 138  ECLISGWGNTLSSGADYPDELQCLDAPVLTQAKCKASYPLKITSKMFCVGFLEGGKDSCQ 197

Query: 202  GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             GDSGGP+VC G+L+G+VSWG   C  K  +PGVYT V  ++ WI++ +
Sbjct: 198  GDSGGPVVCNGQLQGIVSWG-YGCAQKRRPGVYTKVYNYVDWIKDTI 243
```

>gi|51094519|gb|EAL23774.1| G protease, serine, 2 (trypsin 2) [Homo sapiens]
gi|4506147|ref|NP_002761.1| G protease, serine, 2 preproprotein [Homo sapiens]
gi|88942|pir||B25852 trypsin (EC 3.4.21.4) II precursor [validated] - human
gi|1552517|gb|AAC80209.1| G trypsinogen E [Homo sapiens]
gi|2275595|gb|AAC13351.1| G anionic trypsinogen [Homo sapiens]
gi|136413|sp|P07478|TRY2_HUMAN G Trypsin II precursor (Anionic trypsinogen)
gi|521218|gb|AAA61232.1| G trypsinogen
gi|224982|prf||1205235B trypsinogen II
Length = 247

Score = 198 bits (504), Expect = 1e-49
Identities = 95/245 (38%), Positives = 147/245 (60%), Gaps = 4/245 (1%)

```
Query: 6    LTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVL 65
             + + ++    +  A +A   ++ +K+V G  C ++S P+Q +L  SG+  CGG LI  QWV+
Sbjct: 1    MNLLLILTFVAAAVAAPFDDDDKIVGGYICEENSVPYQVSL-NSGYHFCGGSLISEQWVV 59

Query: 66   TAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKF 125
```

```
           +A HC K  +QV LG+HN+    E   ++ I+   + I HP+YN   T DNDI+++ L +P
Sbjct: 60  SAGHCYKSRIQVRLGEHNIEVLEGNEQFINAAKIIRHPKYNSRTLDNDILLIKLSSPAVI 119

Query: 126 SKKIQPLPLKNDCSEENPNCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKI 183
           + ++   + L                I GWG         D+PD +QC D  ++ + +CE +YPGKI
Sbjct: 120 NSRVSAISLPTAPPAAGTESLISGWGNTLSSGADYPDELQCLDAPVLSQAECEASYPGKI 179

Query: 184 TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
           T +M C G ++ G DSCQGDSGGP+V   G L+G+VSWG   C  K +PGVYT V  ++ W
Sbjct: 180 TNNMFCVGFLEGGKDSCQGDSGGPVVSNGELQGIVSWG-YGCAQKNRPGVYTKVYNYVDW 238

Query: 244 IQNIL 248
           I++ +
Sbjct: 239 IKDTI 243
```

>gi|55629564|ref|XP 519441.1| G PREDICTED: similar to trypsinogen C [Pan troglodyte
Length = 247

Score = 198 bits (504), Expect = 1e-49
Identities = 93/227 (40%), Positives = 140/227 (61%), Gaps = 4/227 (1%)

```
Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
           ++ +K+V G  C ++S P+Q +L +   H  CGG LI  QWV++A HC KP++QV LG+HN
Sbjct: 19  DDDDKIVGGYTCEENSVPYQVSLNSGSHF-CGGSLISEQWVVSAGHCYKPHIQVRLGEHN 77

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
           +    E  ++ I+  + I HP+YN   T +NDIM++ L  P    +  +  + L
Sbjct: 78  IEVLEGNEQFINAAKIIRHPKYNRITLNNDIMLIKLSTPAVINAHVSNISLPTAPPAAGT 137

Query: 144 NCQILGWGK--MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
            C I GWG        D+PD +QC D  ++ + +C+ +YP KIT +M C G ++ G DSCQ
Sbjct: 138 ECLISGWGNTLSSGADYPDELQCLDAPVLTQAKCKASYPLKITSNMFCVGFLEGGKDSCQ 197

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           GDSGGP+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 198 GDSGGPVVCNGQLQGIVSWG-YGCAQKRRPGVYTKVYNYVDWIKDTI 243
```

>gi|49259460|pdb|1V2N|T S Chain T, Potent Factor Xa Inhibitor In Complex With Bovir
Variant X(99175190)BT
Length = 223

Score = 198 bits (504), Expect = 1e-49
Identities = 93/222 (41%), Positives = 137/222 (61%), Gaps = 4/222 (1%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
           +V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1   IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
             ++ IS  ++IVHP YN ET++NDIM++ LK+     + ++   + L   C+      C I
Sbjct: 60  GNEQFISASKSIVHPSYNSETYNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
           GWG  K      +PD ++C      ++      C+ A      IT +M CAG ++ G D+CQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSASSFIITSNMFCAGYLEGGKDACQGDSGG 179
```

```
Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           P+VC G+L+G+VSWG    C  K KPGVYT VC ++ WI+  +
Sbjct: 180 PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220
```

```
>gi|3024066|sp|Q28773|KLK1_PAPHA   Kallikrein 1 precursor (Tissue kallikrein)
          (Kidney/pancreas/salivary gland kallikrein)
 gi|871814|gb|AAA73523.1|    tissue kallikrein
         Length = 258

 Score =  198 bits (504), Expect = 1e-49
 Identities = 99/257 (38%), Positives = 147/257 (57%), Gaps = 19/257 (7%)

Query: 8   MKMLALCLVLA---KSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
           M  L LCL L+      A      Q ++V G  C   S P+QAALY       CGG+L+ PQWV
Sbjct: 1   MWFLVLCLALSLGGTGAAPPIQSRIVGGWEC---SQPWQAALYHFSTFQCGGILVHPQWV 57

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN-----------PETHDND 113
           LTAAHC    N Q+ LG+HNL    E    + + V   +   HP +N             E + +D
Sbjct: 58  LTAAHCIGDNYQLWLGRHNLFDDEDTAQFVHVSESFPHPCFNMSLLKNHTRQADEDYSHD 117

Query: 114 IMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLVP 171
           +M++ L   P + +  +Q + L      E     C    GWG +E  N  +PD +QC D+ ++P
Sbjct: 118 LMLLRLTQPAEITDAVQVVELPTQEPEVGSTCLASGWGSIEPENFSYPDDLQCVDLKILP 177

Query: 172 REQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKP 231
            ++C +A++  K+T+ M+CAG ++ G D+C GDSGGPL C G L+G+ SWG +PCGS  KP
Sbjct: 178 NDKCAKAHTQKVTEFMLCAGHLEGGKDTCVGDSGGPLTCDGVLQGVTSWGYIPCGSPNKP 237

Query: 232 GVYTDVCTHIRWIQNIL 248
            V+  V ++++WI++ +
Sbjct: 238 AVFVRVLSYVKWIEDTI 254
```

```
>gi|2136330|pir||I38363   trypsin (EC 3.4.21.4) IV form b precursor - human (fragment
 gi|739993|prf||2004280A   trypsinogen IV
         Length = 259

 Score =  198 bits (503), Expect = 1e-49
 Identities = 94/227 (41%), Positives = 144/227 (63%), Gaps = 5/227 (2%)

Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
           ++ +K+V G  C ++S P+Q +L +  H  CGG LI  QWV++AAHC K   +QV LG+HN
Sbjct: 32  DDDDKIVGGYTC-ENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHN 89

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
           ++  E  ++ I+  + I HP+YN +T DNDIM++ L +P    + ++  + L
Sbjct: 90  IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTAPPAAGT 149

Query: 144 NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
            C I GWG   +  D+PD ++C D  ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 150 ECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 209

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            DSGGP+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 210 RDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 255
```

>gi|3980129|emb|CAA50484.1| G trypsinogen IV b-form [Homo sapiens]
Length = 259

Score = 198 bits (503), Expect = 1e-49
Identities = 94/227 (41%), Positives = 144/227 (63%), Gaps = 5/227 (2%)

```
Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G  C ++S P+Q +L +  H  CGG LI  QWV++AAHC K  +QV LG+HN
Sbjct: 32  DDDDKIVGGYTC-ENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHN 89

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            ++  E  ++ I+  + I HP+YN +T DNDIM++ L +P    + ++  + L
Sbjct: 90  IKVLEGNEQFINAAKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTAPPAAGT 149

Query: 144 NCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
             C I GWG   +   D+PD ++C D  ++ + +C+ +YPGKIT SM C G ++ G DSCQ
Sbjct: 150 ECLISGWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQ 209

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             DSGGP+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 210 RDSGGPVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 255
```

>gi|51539252|gb|AAU06121.1| trypsinogen [Takifugu rubripes]
Length = 235

Score = 197 bits (502), Expect = 2e-49
Identities = 100/230 (43%), Positives = 141/230 (61%), Gaps = 7/230 (3%)

```
Query: 25  EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC--KKPNLQVILGKH 82
            E  +++ G  C   S P+ A+L   G+  CGGVLI+ QWVL+ AHC      +QV+LG+H
Sbjct: 5   EDGRIIGGQECEPHSRPYMASL-NYGYHFCGGVLINKQWVLSVAHCWYNPYAMQVMLGEH 63

Query: 83  NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
            ++R  E  ++ +  D  I HP Y+ +T D+DIM++ L +PV+ ++ + P+ L    C
Sbjct: 64  DVRVFEGTEQLMKTDTIIWHPDYDYQTLDHDIMLIKLFHPVEVTESVAPISLPTGCPYGG 123

Query: 143 PNCQILGWGKM-ENGD--FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDS 199
              C + GWG    +GD   P+ +QC DV  V  E CE+AYPG IT+ MVCAG M  G D+
Sbjct: 124 MPCSVSGWGNTASSGDAIMPNRLQCLDVPAVSNEDCEKAYPGMITRRMVCAGYMDGGRDA 183

Query: 200 CQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
            C GDSG PLVC G ++GLVSWG   C   E PGVY  VC   + WI+++L+
Sbjct: 184 CNGDSGSPLVCFGEVQGLVSWG-QGCALPEYPGVYVKVCEFLYWIEDVLQ 232
```

>gi|4809136|gb|AAD30107.1| trypsinogen-like serine protease [Notothenia coriiceps]
Length = 249

Score = 197 bits (502), Expect = 2e-49
Identities = 105/247 (42%), Positives = 144/247 (58%), Gaps = 8/247 (3%)

```
Query: 8   MKMLALCLVL-AKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLT 66
            M +LAL L++ A +A    E  ++V G  C   S P+ A+L   G+  CGGVLI+ QWVL+
```

```
Sbjct: 1   MTLLALLLLIGAAAAVPREDGRIVGGYECSPHSRPYMASL-NYGYHFCGGVLINNQWVLS 59

Query: 67  AAHC--KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
            AHC       +QVILG HNLR  E  ++ +  D  I HP Y+ +T D DIM++ L +PV+
Sbjct: 60  VAHCWYNPYYMQVILGDHNLRVFEGTEQLMKTDTIIWHPSYDYQTLDFDIMLIKLYHPVE 119

Query: 125 FSKKIQPLPLKNDCSEENPNCQILGWGKMENGD---FPDTIQCADVHLVPREQCERAYPG 181
            ++ + P+PL   C      +C + GWG     G      P  +QC +V +V  + CE AYPG
Sbjct: 120 VTEAVAPIPLPTRCPYGGLSCSVSGWGNTNLGGEVYMPTLLQCLNVPIVDLQVCENAYPG 179

Query: 182 KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHI 241
            I+  MVCAG M+ G D+C GDSG PLVC G ++GLVSWG   C      PGVY  +C
Sbjct: 180 MISPRMVCAGYMEGGKDACNGDSGSPLVCDGEVQGLVSWG-QGCAEPNYPGVYVKLCEFH 238

Query: 242 RWIQNIL 248
            W + +L
Sbjct: 239 SWFEEVL 245
```

>gi|971196|gb|AAA75001.1| G trypsinogen
Length = 237

Score = 197 bits (502), Expect = 2e-49
Identities = 94/235 (40%), Positives = 143/235 (60%), Gaps = 3/235 (1%)

```
Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPN 74
           +  A +A  +E +K+V G  C K+S   +Q +L  SG+  CGG L++  WV++AAHC K
Sbjct: 2   IAAAYAAPIDEDDKIVGGYECRKNSVAYQVSL-NSGYHFCGGSLVNENWVVSAAHCYKSR 60

Query: 75  LQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           + V LG+HN+R  E  ++ IS  R I HP Y+    DNDIM++ L  P   ++ +QP+ L
Sbjct: 61  VVVRLGEHNIRANEGTEQFISSSRVIRHPNYSSYNIDNDIMLIKLSKPATLNQYVQPVAL 120

Query: 135 KNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDM 193
            + C+      C++ GWG  M +    + +QC ++ ++   CE +YPG IT +M CAG +
Sbjct: 121 PSSCAAAGTMCKVSGWGNTMSSTADRNKLQCLNIPILSDRDCENSYPGMITDAMFCAGYL 180

Query: 194 KEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           + G DSCQGDSGGP+VC    L+G+VSWG   C  ++ PGVY  VC    W+++ +
Sbjct: 181 EGGKDSCQGDSGGPVVCNNELQGVVSWG-YGCAERDHPGVYAKVCLFNDWLESTM 234
```

>gi|13994131|ref|NP_113711.1| G nerve growth factor, gamma [Rattus norvegicus]
gi|51261180|gb|AAH78784.1| G Nerve growth factor, gamma [Rattus norvegicus]
gi|220794|dbj|BAA00346.1| G kallikrein precursor [Rattus norvegicus]
gi|67565|pir||KQRTP tissue kallikrein (EC 3.4.21.35) precursor - rat
gi|205030|gb|AAA41464.1| G PS kallikrein
gi|364506|prf||1508215A true tissue kallikrein
Length = 265

Score = 197 bits (501), Expect = 2e-49
Identities = 98/260 (37%), Positives = 148/260 (56%), Gaps = 16/260 (6%)

```
Query: 6   LTMKMLALCLVLA---KSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQ 62
           +TM  L L L L+      A    Q +VV G  C   +S P+Q A+Y   G  LCGGVLIDP
Sbjct: 3   VTMWFLILFLALSLGRNDAAPPVQSRVVGGYNCEMNSQPWQVAVYYFGEYLCGGVLIDPS 62
```

```
Query: 63   WVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPET-----------HD 111
            WV+TAAHC   N QV LG++NL + E F +    V ++  HP +N +            +
Sbjct: 63  WVITAAHCATDNYQVWLGRNNLYEDEPFAQHRLVSQSFPHPGFNQDLIWNHTRQPGDDYS 122

Query: 112 NDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKM--ENGDFPDTIQCADVHL 169
            ND+M++HL  P    +  ++ + L  +  +     C   GWG +   +  +  D +QC ++ L
Sbjct: 123 NDLMLLHLSQPADITDGVKVIDLPIEEPKVGSTCLASGWGSITPDGLELSDDLQCVNIDL 182

Query: 170 VPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKE 229
            +  E+C  A+  ++T  M+CAG+M  G D+C+GDSGGPL+C G L+G+ SWG  PCG  +
Sbjct: 183 LSNEKCVEAHKEEVTDLMLCAGEMDGGKDTCKGDSGGPLICNGVLQGITSWGFNPCGEPK 242

Query: 230 KPGVYTDVCTHIRWIQNILR 249
            KPG+YT +     WI+ +++
Sbjct: 243 KPGIYTKLIKFTPWIKEVMK 262
```

>gi|34856011|ref|XP_214947.2| G similar to Glandular kallikrein 10 precursor (Tissu
(T-kininogenase) (K10) (Proteinase B) (Endopeptidase K)
[Rattus norvegicus]
Length = 374

Score = 197 bits (501), Expect = 2e-49
Identities = 101/265 (38%), Positives = 150/265 (56%), Gaps = 19/265 (7%)

```
Query: 2   PMKMLTMKML-ALCLVLAKS---AWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGV 57
            P K L+ KML  + L L  S   A    Q ++V G  C K+S P+Q A+       LCGGV
Sbjct: 109 PDKSLSAKMLQCVDLTLMSSDVYAAPPGQSRIVGGYKCEKNSQPWQVAIINE--YLCGGV 166

Query: 58  LIDPQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP---------- 107
            LIDP WV+TAAHC        V+LG++NL + E F +    V+++  HP Y P
Sbjct: 167 LIDPSWVITAAHCYSNYYHVLLGRNNLFEDEPFAQYRFVNQSFPHPDYKPFLMRNHTRQR 226

Query: 108 -ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQC 164
              + + ND+M++HL  P    +  ++ + L  +  +     C   GWG   +  N + PD +QC
Sbjct: 227 GDDYSNDLMLLHLSEPADITDGVKVIDLPTEEPKVGSTCLASGWGSTKPLNWELPDDLQC 286

Query: 165 ADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMP 224
             ++HL+   E+C  AY  K+T  M+CAG+M    D+C+GDSGGPL+C G L+G+ SWG++P
Sbjct: 287 VNIHLLSNEKCIEAYEQKVTDLMLCAGEMDGRKDTCKGDSGGPLICDGVLQGITSWGNVP 346

Query: 225 CGSKEKPGVYTDVCTHIRWIQNILR 249
            C       PGVYT +     WI+ +++
Sbjct: 347 CAEPYNPGVYTKLIKFTSWIKEVMK 371
```

>gi|57113389|ref|XP_537905.1| G PREDICTED: similar to trypsin (EC 3.4.21.4) precurs
dog [Canis familiaris]
Length = 769

Score = 197 bits (501), Expect = 2e-49
Identities = 93/215 (43%), Positives = 141/215 (65%), Gaps = 4/215 (1%)

```
Query: 23  SEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKH 82
            +++ +K+V G  C ++S P+Q +L  +G+  CGG LI  QWV++AAHC K  +QV LG++
Sbjct: 262 TDDDDKIVGGYTCEENSVPYQVSL-NAGYHFCGGSLISDQWVVSAAHCYKSRIQVRLGEY 320
```

```
Query: 83   NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
            N+    E  ++ I+   + I HP YN    DNDIM++ L +P    + ++   + L   C+
Sbjct: 321 NIDVLEGNEQFINSAKVIRHPNYNSWILDNDIMLIKLSSPAVLNARVATISLPRACAAPG 380

Query: 143 PNCQILGWGK-MENG-DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
              C I GWG   + +G ++P+ +QC D   ++ + QCE +YPG+IT++M+CAG ++ G DSC
Sbjct: 381 TQCLISGWGNTLSSGTNYPELLQCLDAPILTQAQCEASYPGQITENMICAGFLEGGKDSC 440

Query: 201 QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYT 235
            QGDSGGP+VC G L+G+VSWG    C  K KPGVYT
Sbjct: 441 QGDSGGPVVCNGELQGIVSWG-YGCAQKNKPGVYT 474
```

>gi|33126583|gb|AAL14244.1| G protease serine 2 isoform B [Homo sapiens]
Length = 261

```
 Score =  197 bits (501), Expect = 2e-49
 Identities = 93/227 (40%), Positives = 139/227 (61%), Gaps = 4/227 (1%)

Query: 24  EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHN 83
            ++ +K+V G   C ++S P+Q +L  SG+   CGG LI   QWV++A HC K   +QV LG+HN
Sbjct: 33  DDDDKIVGGYICEENSVPYQVSL-NSGYHFCGGSLISEQWVVSAGHCYKSRIQVRLGEHN 91

Query: 84  LRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            +    E  ++ I+   + I HP+YN   T DNDI+++ L +P    + ++   + L
Sbjct: 92  IEVLEGNEQFINAAKIIRHPKYNSRTLDNDILLIKLSSPAVINSRVSAISLPTAPPAAGT 151

Query: 144 NCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQ 201
               I GWG       D+PD +QC D   ++ + +CE +YPGKIT +M C G ++ G DSCQ
Sbjct: 152 ESLISGWGNTLSSGADYPDELQCLDAPVLSQAECEASYPGKITNNMFCVGFLEGGKDSCQ 211

Query: 202 GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            GDSGGP+V  G L+G+VSWG   C  K +PGVYT V   ++ WI++ +
Sbjct: 212 GDSGGPVVSNGELQGIVSWG-YGCAQKNRPGVYTKVYNYVDWIKDTI 257
```

>gi|20988034|gb|AAH30260.1| G PRSS2 protein [Homo sapiens]
Length = 239

```
 Score =  197 bits (501), Expect = 2e-49
 Identities = 95/241 (39%), Positives = 144/241 (59%), Gaps = 4/241 (1%)

Query: 6   LTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVL 65
            + + ++    +  A +A  ++ +K+V G   C ++S P+Q +L  SG+   CGG LI   QWV+
Sbjct: 1   MNLLLILTFVAAAVAAPFDDDDKIVGGYICEENSVPYQVSL-NSGYHFCGGSLISEQWVV 59

Query: 66  TAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKF 125
            +A HC K   +QV LG+HN+    E  ++ I+   + I HP+YN   T DNDI+++ L +P
Sbjct: 60  SAGHCYKSRIQVRLGEHNIEVLEGNEQFINAAKIIRHPKYNSRTLDNDILLIKLSSPAVI 119

Query: 126 SKKIQPLPLKNDCSEENPNCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKI 183
            + ++   + L                I GWG       D+PD +QC D   ++ + +CE +YPGKI
Sbjct: 120 NSRVSAISLPTAPPAAGTESLISGWGNTLSSGADYPDELQCLDAPVLSQAECEASYPGKI 179

Query: 184 TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
            T +M C G ++ G DSCQGDSGGP+V  G L+G+VSWG   C  K +PGVYT V   ++ W
```

```
Sbjct: 180 TNNMFCVGFLEGGKDSCQGDSGGPVVSNGELQGIVSWG-YGCAQKNRPGVYTKVYNYVDW 238

Query: 244 I 244
           I
Sbjct: 239 I 239
```

>gi|56611148|gb|AAH87751.1| Hypothetical LOC496633 [Xenopus tropicalis]
gi|58332104|ref|NP_001011204.1| hypothetical LOC496633 [Xenopus tropicalis]
Length = 249

Score = 197 bits (501), Expect = 2e-49
Identities = 92/248 (37%), Positives = 142/248 (57%), Gaps = 6/248 (2%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M +  L  +    +A    + +K+V G  C   S P+Q          + CGG L+ P+W+++A
Sbjct: 2    MPLWILLFLAVAAAAPLDDDKIVGGYECTPHSQPWQVYFTQENQVFCGGSLVTPRWIISA 61

Query: 68   AHCKKPNLQVI--LGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKF 125
            AHC +     ++   LG H+L + E   ++ I V+     H  Y      D+DIM+V L  P ++
Sbjct: 62   AHCYRTPKTLVAHLGDHDLTKEEGTEQHIQVENIYKHFSYKDNDVDHDIMLVKLAKPAQY 121

Query: 126  SKKIQPLPLKNDCSEENPNCQILGWGKMEN---GDFPDTIQCADVHLVPREQCERAYPGK 182
            ++ +QP+P+     C  E    C + G+G M +    G+FPD +QC DV ++     C+ +Y G
Sbjct: 122  NQYVQPIPVARSCPREGTECLVSGYGNMRSDNIGEFPDRLQCVDVPVLSDSSCKASYRGL 181

Query: 183  ITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
             T++M CAG ++ G DSCQ DSGGPLVC G L G+VSWG   C   +   PGVY  VC ++
Sbjct: 182  FTENMFCAGFLEGGKDSCQVDSGGPLVCNGELYGVVSWG-QGCAERNAPGVYAKVCNYLG 240

Query: 243  WIQNILRN 250
            W+Q+I+ N
Sbjct: 241  WVQDIIEN 248
```

>gi|3452120|gb|AAC32752.1| trypsinogen 2 precursor [Pseudopleuronectes americanus]
Length = 242

Score = 197 bits (501), Expect = 2e-49
Identities = 94/242 (38%), Positives = 144/242 (59%), Gaps = 4/242 (1%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M+ L   L++  +A++ E +K+V G  C   S  Q +L SG+  CGG L++  WV++A
Sbjct: 1    MRSLVFVLLIG-AAFALEDDKIVGGYECTPHSQAHQVSL-NSGYHFCGGSLVNENWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K  ++V +G+H +R  E  ++ +S  R I HP Y+    DNDIM++ L  P   ++
Sbjct: 59   AHCYKSRVEVRMGEHKIRVNEGTEQFVSSSRVIRHPNYDSWNIDNDIMLIKLSKPATLNQ 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQS 186
             ++ + L + C+      C++ GWG  M + D  D +QC D+ ++    C  AYPG IT S
Sbjct: 119  YVKTVALPSSCAPAGTMCKVSGWGNTMSSADNGDLLQCLDIPILSFSDCNNAYPGMITDS 178

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M CAG ++ G DSCQGDSGGP++C G L+G+VSWG   C   +   PGVY  VC    W+++
Sbjct: 179  MFCAGYLEGGKDSCQGDSGGPVICNGELQGVVSWG-YGCAERGNPGVYAKVCLFNDWLES 237
```

```
Query: 247 IL 248
            +
Sbjct: 238 TM 239
```

>gi|51539247|gb|AAU06120.1| trypsinogen [Takifugu rubripes]
Length = 247

```
 Score =  197 bits (500), Expect = 3e-49
 Identities = 99/242 (40%), Positives = 148/242 (61%), Gaps = 6/242 (2%)

Query: 11  LALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC 70
            L L  VL  +A +   +++V G  C   S P+Q ++    G+  CGG LI+ QW+++AAHC
Sbjct: 4   LVLLTVLGAAAAAPTDDRIVGGYECTAHSQPWQVSI-NIGYHYCGGSLINDQWIISAAHC 62

Query: 71  -KKPNLQV-ILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
             + P  Q+ ILG H++   E  ++ +SVD    H  Y+  T D DIM++ L +PV  ++
Sbjct: 63  WQNPYTQIAILGDHHIWMHEGTEQYMSVDAIYWHQSYDYTTLDYDIMLLKLAHPVTQNQY 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQS 186
            ++P+ L   C E    C + GWG + + D   P  +QC +V ++  ++C+ +YPGKIT+
Sbjct: 123 VKPVALPKACPEAGDKCTVSGWGNIYSDDVFNPFNLQCVEVPILSDKECDNSYPGKITER 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            MVCAG ++ G D+CQGDSGGPLVC   L G+VSWG  C    PGVYT VC+ + WIQ+
Sbjct: 183 MVCAGYLEGGKDACQGDSGGPLVCNNELHGIVSWG-QGCAQPNYPGVYTKVCSLLPWIQD 241

Query: 247 IL 248
            +L
Sbjct: 242 VL 243
```

>gi|49259469|pdb|1V2W|T Chain T, Trypsin Inhibitor In Complex With Bovine Trypsi
X(Ssai)bt.B4
gi|49259468|pdb|1V2V|T Chain T, Benzamidine In Complex With Bovine Trypsin Variant
Bt.C1
gi|49259467|pdb|1V2U|T Chain T, Benzamidine In Complex With Bovine Trypsin Varinat
Bt.D1
Length = 223

```
 Score =  197 bits (500), Expect = 3e-49
 Identities = 93/222 (41%), Positives = 135/222 (60%), Gaps = 4/222 (1%)

Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+  E
Sbjct: 1   IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
             ++ IS  ++IVHP YN  T +NDIM++ LK+   + ++  + L  C+     C I
Sbjct: 60  GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K    +PD ++C    ++   C+ A   IT +M CAG ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSASSAIITSNMFCAGYLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG  C  K KPGVYT VC ++ WI+  +
```

```
Sbjct: 180  PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220
```

>gi|20149993|pdb|1H4W|A Chain A, Structure Of Human Trypsin Iv (Brain Trypsin)
Length = 224

Score = 197 bits (500), Expect = 3e-49
Identities = 93/222 (41%), Positives = 140/222 (63%), Gaps = 4/222 (1%)

```
Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             +V G  C ++S P+Q +L +   H  CGG LI  QWV++AAHC K  +QV LG+HN++  E
Sbjct: 1    IVGGYTCEENSLPYQVSLNSGSHF-CGGSLISEQWVVSAAHCYKTRIQVRLGEHNIKVLE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ I+  + I HP+YN +T DNDIM++ L +P    + ++   + L          C I
Sbjct: 60   GNEQFINAVKIIRHPKYNRDTLDNDIMLIKLSSPAVINARVSTISLPTAPPAAGTECLIS 119

Query: 149  GWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
             GWG    +  D+PD ++C D   ++ + +C+ +YPGKIT SM C G ++ G DSCQ DSGG
Sbjct: 120  GWGNTLSFGADYPDELKCLDAPVLTQAECKASYPGKITNSMFCVGFLEGGKDSCQRDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             P+VC G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 180  PVVCNGQLQGVVSWGH-GCAWKNRPGVYTKVYNYVDWIKDTI 220
```

>gi|223207|prf||0608151A kallikrein B
Length = 232

Score = 197 bits (500), Expect = 3e-49
Identities = 91/228 (39%), Positives = 134/228 (58%), Gaps = 8/228 (3%)

```
Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
             ++ G  C K+SHP+Q A+Y       CGGVL++P+WVLTAAHCK  N +V   +HNL + E
Sbjct: 1    IIGGRECEKNSHPWQVAIYHYSSFQCGGVLVNPKWVLTAAHCKNDNYEVGWLRHNLFENE 60

Query: 89   TFQRQISVDRTIVHPRYN----PETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPN 144
               +   V      HP +N       + + +D+M++ L++P K +  ++ L L     E
Sbjct: 61   NTAQFFGVTADFPHPGFNLSADGKDYSHDLMLLRLQSPAKITDAVKVLELPTQEPELGST 120

Query: 145  CQILGWGKMENG----DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
             C+   GWG +E G     +FPD IQC  + L+     C  A P K+T+SM+CAG +  G D+C
Sbjct: 121  CEASGWGSIEPGPDDFEFPDEIQCVQLTLLQNTFCAHABPBKVTESMLCAGYLPGGKDTC 180

Query: 201  QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
              GDSGGPL+C G  +G+ SWG  PCGS  KP +YT +  ++ WI + +
Sbjct: 181  MGDSGGPLICNGMWQGITSWGHTPCGSANKPSIYTKLIFYLDWIBBTI 228
```

>gi|13516893|dbj|BAB40330.1| trypsinogen II [Engraulis japonicus]
Length = 241

Score = 196 bits (499), Expect = 4e-49
Identities = 94/234 (40%), Positives = 141/234 (60%), Gaps = 3/234 (1%)

```
Query: 15   LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPN 74
```

```
           LVL  +A++E+ +K+V G  C   S P Q +L  SG+  CGG L+   WV++AAHC K
Sbjct: 7   LVLLGAAFAED-DKIVGGYECQPYSQPHQVSL-NSGYHFCGGSLVSDSWVVSAAHCYKSR 64

Query: 75  LQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           ++V +G+H++  TE  ++ I   R I HP+Y+    DNDIM++ L  P   ++ +Q + L
Sbjct: 65  VEVRMGEHHIGMTEGNEQFIDSSRVIRHPQYDSYNIDNDIMLIKLSKPATLNQYVQTVAL 124

Query: 135 KNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMK 194
            + C+      C + GWG   +    D +QC  + ++    C+ +YPG IT+SM CAG ++
Sbjct: 125 PSSCAPAGTMCLVSGWGNTMSNVSGDKLQCLQIPILSDRDCKNSYPGMITESMFCAGYLE 184

Query: 195 EGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            G DSCQGDSGGP+VC G L+G+VSWG   C  ++ PGVY  VC    WI + +
Sbjct: 185 GGKDSCQGDSGGPVVCNGELQGIVSWG-YGCAERDHPGVYAKVCLFNDWIDSTM 237
```

>gi|1399811|gb|AAB57732.1| pretrypsinogen-like serine protease [Dissostichus mawsor
Length = 249

```
Score =  196 bits (499), Expect = 4e-49
Identities = 102/247 (41%), Positives = 147/247 (59%), Gaps = 8/247 (3%)

Query: 8   MKMLALCLVL-AKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLT 66
           M +LAL L++ A +A   E  +++ G  C   S P+ A+L   G+  CGGVLI+ QWVL+
Sbjct: 1   MTLLALLLLIGAAAAVPREDGRIIGGYECSPHSRPYMASL-NYGYHFCGGVLINNQWVLS 59

Query: 67  AAHC--KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
            AHC     ++QVILG HNLR  E   ++ +  +  I HP Y+ +T D DIM++ L +PV+
Sbjct: 60  VAHCWYNPYSMQVILGDHNLRVFEGTEQLMKTNTIIWHPSYDYQTLDFDIMLIKLYHPVE 119

Query: 125 FSKKIQPLPLKNDCSEENPNCQILGWGKMENGD---FPDTIQCADVHLVPREQCERAYPG 181
            ++ + P+PL   C      +C + GWG + G      P  +QC +V +V ++ CE  YPG
Sbjct: 120 VTEAVAPIPLPTSCPYGGLSCSVSGWGIAKLGGEAYMPTLLQCLNVPIVDQQVCENTYPG 179

Query: 182 KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHI 241
            I+ +MVCAG M+ G D+C GDSG PLVC G ++GLVSWG   C      PGVY  +C
Sbjct: 180 LISTTMVCAGYMEGGKDACNGDSGSPLVCDGEVQGLVSWG-QGCAEPNYPGVYVKLCEFH 238

Query: 242 RWIQNIL 248
            W + +L
Sbjct: 239 SWFEEVL 245
```

>gi|58257842|gb|AAW69361.1| Try4 [Macaca mulatta]
Length = 248

```
Score =  196 bits (499), Expect = 4e-49
Identities = 95/234 (40%), Positives = 146/234 (62%), Gaps = 5/234 (2%)

Query: 18  AKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQV 77
           A +A  ++ +K+V G  C ++S P+Q +L   G+  CGG LI+ QWV++AAHC KP +QV
Sbjct: 13  AVAAPFDDDDKIVGGYTCEENSVPYQVSL-NYGYHFCGGSLINKQWVVSAAHCYKPRIQV 71

Query: 78  ILGKHNLRQTETFQRQISVDRTIVHPRYNP-ETHDNDIMMVHLKNPVKFSKKIQPLPLKN 136
            LG+HN+    E  ++ I+   + I HP+YN  + ++NDIM++ L  P   + ++  + L
Sbjct: 72  RLGEHNIEVLEGTEQFINAAKIIPHPKYNEVKKYNNDIMLIKLSTPAVINARVSTISLPT 131
```

```
Query: 137 DCSEENPNCQILGWGK--MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMK 194
                    C I GWG        D+PD ++C D   ++ + +CE +YPGKIT +M C G ++
Sbjct: 132 APPAPGTVCLISGWGNTLSSGADYPDELKCLDAPVLTQAECEASYPGKITSNMFCVGFLE 191

Query: 195 EGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
             G DSCQGDSGGP+V  G+L+G+VSWG   C  K +PGVYT V  ++ WI++ +
Sbjct: 192 GGKDSCQGDSGGPVVYNGQLQGVVSWG-YGCAQKNRPGVYTKVYNYLAWIKDTI 244
```

>gi|49259466|pdb|1V2T|T Chain T, Trypsin Inhibitor In Complex With Bovine Trypsin X(Ssfi.Glu)bt.B4
gi|49259465|pdb|1V2S|T Chain T, Benzamidine In Complex With Bovine Trypsin Variant X(Ssfi.Glu)bt.D1
Length = 223

Score = 196 bits (499), Expect = 4e-49
Identities = 93/222 (41%), Positives = 136/222 (61%), Gaps = 4/222 (1%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1   IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ IS  ++IVHP YN  T +NDIM++ LK+    + ++  + L   C+      C I
Sbjct: 60  GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K      +PD ++C     ++     C+ A     IT +M CAG ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSASSFIITSNMFCAGYLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG+  C  K KPGVYT VC ++ WI+  +
Sbjct: 180 PVVCSGKLQGIVSWGE-GCAQKNKPGVYTKVCNYVSWIKQTI 220
```

>gi|1213631|emb|CAA40068.1| trypsin [Pleuronectes platessa]
gi|7435607|pir||T01779 trypsin (EC 3.4.21.4) - plaice
Length = 250

Score = 196 bits (498), Expect = 5e-49
Identities = 105/248 (42%), Positives = 144/248 (58%), Gaps = 9/248 (3%)

```
Query: 8   MKMLALCLVL-AKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLT 66
            M++LAL L++ A  A   E  +++ G  C   S PF A+L   G+  CGGVLI+ QWVL+
Sbjct: 1   MRLLALLLMVGAAVAVPREDGRIIGGHECAAHSRPFMASL-NYGYHFCGGVLINNQWVLS 59

Query: 67  AAHC--KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
             AHC      +QV+LG+H+LR+ E   ++ +   D  I HP Y+ +T D DIM++ L +PV+
Sbjct: 60  VAHCWYNPYAMQVMLGEHDLRKFEGTEQLMKTDTIIWHPNYDYQTLDFDIMLIKLYHPVE 119

Query: 125 FSKKIQPLPLKNDCSEENPNCQILGWGKM-ENGD---FPDTIQCADVHLVPREQCERAYP 180
             S  + P+PL   C       C + GWG     +GD     P  +QC DV +V  EQC ++YP
Sbjct: 120 VSHAVGPIPLPTSCPVAGTPCSVSGWGNTARDGDEVYLPTLLQCMDVPIVDEEQCMKSYP 179

Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
              I+  MVCAG M    D+C GDSG PLVC G + GLVSWG   C      PGVY  +C
Sbjct: 180 DMISPRMVCAGFMDGSRDACNGDSGSPLVCRGEVYGLVSWG-QGCAQPNYPGVYVKLCEF 238
```

```
Query: 241 IRWIQNIL 248
           + WI+  L
Sbjct: 239 LGWIERTL 246
```

>gi|2102686|gb|AAB57728.1| preprotrypsin-like protease [Dissostichus mawsoni]
Length = 249

Score = 196 bits (498), Expect = 5e-49
Identities = 102/247 (41%), Positives = 147/247 (59%), Gaps = 8/247 (3%)

```
Query: 8   MKMLALCLVL-AKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLT 66
            M +LAL L++ A +A    E  +++ G  C    S P+ A+L   G+L C GVLI+ QWVL+
Sbjct: 1   MTLLALLLLIGAAAAVPREDGRIIGGYECSPHSRPYMASL-NYGYLFCDGVLINNQWVLS 59

Query: 67  AAHC--KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
             AHC      ++QVILG HNLR  E  ++ +  +  I HP Y+ +T D DIM++ L +PV+
Sbjct: 60  VAHCWYNPYSMQVILGDHNLRVFEGTEQLMKTNTIIWHPSYDYQTLDFDIMLIKLYHPVE 119

Query: 125 FSKKIQPLPLKNDCSEENPNCQILGWGKMENGD---FPDTIQCADVHLVPREQCERAYPG 181
             ++ + P+PL   C     +C + GWG  + G      P  +QC +V +V ++ CE  YPG
Sbjct: 120 VTEAVAPIPLPTSCPYGGLSCSVSGWGIAKLGGEAYMPTLLQCLNVPIVVQQVCENTYPG 179

Query: 182 KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHI 241
             I+ +MVCAG M+ G D+C GDSG PLVC G ++GLVSWG   C      PGVY  +C
Sbjct: 180 LISTTMVCAGYMEGGKDACNGDSGSPLVCDGEVQGLVSWG-QGCAEPNYPGVYVKLCEFH 238

Query: 242 RWIQNIL 248
             W + +L
Sbjct: 239 SWFEEVL 245
```

>gi|481641|pir||S39048 trypsin (EC 3.4.21.4) X - Atlantic cod
gi|2499867|sp|Q91041|TRYX_GADMO Trypsin X precursor
Length = 241

Score = 196 bits (498), Expect = 5e-49
Identities = 97/240 (40%), Positives = 142/240 (59%), Gaps = 3/240 (1%)

```
Query: 10  MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            M +L  VL   A   E++K+V G  C + S   Q +L  SG+  CGG L+   WV++AAH
Sbjct: 1   MKSLIFVLLLGAVFAEEDKIVGGYECTRHSQAHQVSL-NSGYHFCGGSLVSKDWVVSAAH 59

Query: 70  CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C K  L+V LG+H++R  E  ++ IS    I HP Y+    DNDIM++ L  P   ++ +
Sbjct: 60  CYKSVLRVRLGEHHIRVNEGTEQFISSSSVIRHPNYSSYNIDNDIMLIKLTEPATLNQYV 119

Query: 130 QPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMV 188
             + L  +C+ +   C + GWG  M + D  D +QC ++ ++     C  +YPG ITQSM
Sbjct: 120 HAVALPTECAADATMCTVSGWGNTMSSVDDGDKLQCLNLPILSHADCANSYPGMITQSMF 179

Query: 189 CAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            CAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C  ++ PGVY  VC   W+++ +
Sbjct: 180 CAGYLEGGKDSCQGDSGGPVVCNGVLQGVVSWG-YGCAERDNPGVYAKVCVLSGWVRDTM 238
```

>gi|49259464|pdb|1V2R|T Chain T, Trypsin Inhibitor In Complex With Bovine Trypsin
X(Ssri)bt.B4
gi|49259456|pdb|1V2J|T Chain T, Benzamidine In Complex With Bovine Trypsin Variant
Bt.C1
Length = 223

Score = 196 bits (498), Expect = 5e-49
Identities = 93/222 (41%), Positives = 135/222 (60%), Gaps = 4/222 (1%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1   IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ IS  ++IVHP YN  T +NDIM++ LK+     + ++  + L   C+      C I
Sbjct: 60  GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K      +PD ++C     ++     C+ A     IT +M CAG ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSASSRIITSNMFCAGYLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG   C  K KPGVYT VC ++ WI+  +
Sbjct: 180 PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220
```

>gi|49259463|pdb|1V2Q|T Chain T, Trypsin Inhibitor In Complex With Bovine Trypsin
X(Sswi)bt.B4
Length = 223

Score = 196 bits (498), Expect = 5e-49
Identities = 93/222 (41%), Positives = 135/222 (60%), Gaps = 4/222 (1%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C  ++ P+Q +L  SG+  CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1   IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89  TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ IS  ++IVHP YN  T +NDIM++ LK+     + ++  + L   C+      C I
Sbjct: 60  GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149 GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K      +PD ++C     ++     C+ A     IT +M CAG ++ G DSCQGDSGG
Sbjct: 120 GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSASSWIITSNMFCAGYLEGGKDSCQGDSGG 179

Query: 207 PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG   C  K KPGVYT VC ++ WI+  +
Sbjct: 180 PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220
```

>gi|42543835|pdb|1UTM|A Chain A, Trypsin Specificity As Elucidated By Lie Calcula
X-Ray Structures And Association Constant Measurements
gi|42543834|pdb|1UTL|M Chain M, Trypsin Specificity As Elucidated By Lie Calculati
X-Ray Structures And Association Constant Measurements
gi|42543833|pdb|1UTK|A Chain A, Trypsin Specificity As Elucidated By Lie Calculati

```
        X-Ray Structures And Association Constant Measurements
gi|42543832|pdb|1UTJ|A  Chain A, Trypsin Specificity As Elucidated By Lie Calculati
        X-Ray Structures And Association Constant Measurements
        Length = 242

 Score =  196 bits (498), Expect = 5e-49
 Identities = 97/241 (40%), Positives = 142/241 (58%), Gaps = 4/241 (1%)

Query: 10  MLALCLVLA-KSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            M++L  VL   +A++ E +K+V G  C   S P Q +L  SG+  CGG L++  WV++AA
Sbjct: 1   MISLVFVLLIGAAFATEDDKIVGGYECKPYSQPHQVSL-NSGYHFCGGSLVNENWVVSAA 59

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  ++V LG+HN++ TE  ++ IS  R I HP Y+    DNDIM++ L  P   +
Sbjct: 60  HCYKSRVEVRLGEHNIKVTEGSEQFISSSRVIRHPNYSSYNIDNDIMLIKLSKPATLNTY 119

Query: 129 IQPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 187
            +QP+ L   C+     C + GWG  M +     + +QC ++ ++    C  +YPG IT +M
Sbjct: 120 VQPVALPTSCAPAGTMCTVSGWGNTMSSTADSNKLQCLNIPILSYSDCNNSYPGMITNAM 179

Query: 188 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
             CAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C     PGVY  VC    W+ +
Sbjct: 180 FCAGYLEGGKDSCQGDSGGPVVCNGELQGVVSWG-YGCAEPGNPGVYAKVCIFNDWLTST 238

Query: 248 L 248
            +
Sbjct: 239 M 239


>gi|547788|sp|P00758|KLK1_RAT  Glandular kallikrein, pancreatic 1 precursor (Tissu
         (PS kallikrein) (RGK-1)
gi|205009|gb|AAA41462.1|   kallikrein
        Length = 261

 Score =  196 bits (497), Expect = 6e-49
 Identities = 96/254 (37%), Positives = 147/254 (57%), Gaps = 14/254 (5%)

Query: 10  MLALCLVLAKS-AWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L L ++ A    Q +VV G  C  +S P+Q A+Y  G  LCGGVLIDP WV+TAA
Sbjct: 5   ILFLALSLGRNDAAPPVQSRVVGGYNCEMNSQPWQVAVYYFGEYLCGGVLIDPSWVITAA 64

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPET-----------HDNDIMMV 117
            HC   N QV LG++NL + E F +   V ++  HP +N +             + ND+M++
Sbjct: 65  HCATDNYQVWLGRNNLYEDEPFAQHRLVSQSFPHPGFNQDLIWNHTRQPGDDYSNDLMLL 124

Query: 118 HLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKM--ENGDFPDTIQCADVHLVPREQC 175
            HL  P   +  ++ + L  +  +    C   GWG +  +  +  D +QC ++ L+  E+C
Sbjct: 125 HLSQPADITDGVKVIDLPIEEPKVGSTCLASGWGSITPDGLELSDDLQCVNIDLLSNEKC 184

Query: 176 ERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYT 235
              A+  ++T  M+CAG+M  G D+C+GDSGGPL+C G L+G+ SWG  PCG  +KPG+YT
Sbjct: 185 VEAHKEEVTDLMLCAGEMDGGKDTCKGDSGGPLICNGVLQGITSWGFNPCGEPKKPGIYT 244

Query: 236 DVCTHIRWIQNILR 249
             +     WI+ +++
Sbjct: 245 KLIKFTPWIKEVMK 258
```

```
>gi|57037493|ref|XP_541470.1| G PREDICTED: similar to enamel matrix serine proteina
          [Canis familiaris]
         Length = 314

 Score =  196 bits (497), Expect = 6e-49
 Identities = 93/223 (41%), Positives = 130/223 (58%), Gaps = 1/223 (0%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQT- 87
            +++G  C    S P+QAAL+T      CGGVL+ PQWVL+AAHC + +   + LG H+L
Sbjct: 91   IINGEDCSPHSQPWQAALFTEDEFFCGGVLVHPQWVLSAAHCFQNSYTIGLGLHSLEPNQ 150

Query: 88   ETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQI 147
            E    R +  D +I HP YN      ND+M++ LK  V  S  IQ + + + C     +C +
Sbjct: 151  EPGSRMMETDLSIQHPEYNKPFVANDLMLIKLKESVSESDTIQNISIASQCPTAGDSCLV 210

Query: 148  LGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGP 207
             GWG++ +G  P  +QC ++ +VP E C    Y      SM CAG ++  DSC GDSGGP
Sbjct: 211  SGWGQLIDGRQPQVLQCVNISVVPEETCNAFYAPVYHPSMFCAGGGQDRKDSCHGDSGGP 270

Query: 208  LVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            LVC G L+GLVS+G   CG    PGVYT++C    WIQ  +++
Sbjct: 271  LVCNGSLQGLVSFGQAQCGLPHVPGVYTNLCKFKDWIQKTIQD 313


 >gi|49259462|pdb|1V2P|T S Chain T, Trypsin Inhibitor In Complex With Bovine Trypsir
          X(Ssyi)bt.A4
 gi|49259461|pdb|1V2O|T S Chain T, Trypsin Inhibitor In Complex With Bovine Trypsin V
          X(Ssyi)bt.B4
         Length = 223

 Score =  196 bits (497), Expect = 6e-49
 Identities = 93/222 (41%), Positives = 135/222 (60%), Gaps = 4/222 (1%)

Query: 29   VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
            +V G  C   ++ P+Q +L  SG+   CGG LI+ QWV++AAHC K  +QV LG+ N+   E
Sbjct: 1    IVGGYTCGANTVPYQVSL-NSGYHFCGGSLINSQWVVSAAHCYKSGIQVRLGEDNINVVE 59

Query: 89   TFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQIL 148
              ++ IS  ++IVHP YN  T +NDIM++ LK+      + ++  + L   C+      C I
Sbjct: 60   GNEQFISASKSIVHPSYNSNTLNNDIMLIKLKSAASLNSRVASISLPTSCASAGTQCLIS 119

Query: 149  GWG--KMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGG 206
            GWG  K        +PD ++C     ++      C+ A     IT +M CAG ++ G DSCQGDSGG
Sbjct: 120  GWGNTKSSGTSYPDVLKCLKAPILSDSSCKSASSYIITSNMFCAGYLEGGKDSCQGDSGG 179

Query: 207  PLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            P+VC G+L+G+VSWG   C  K KPGVYT VC ++ WI+ +
Sbjct: 180  PVVCSGKLQGIVSWGS-GCAQKNKPGVYTKVCNYVSWIKQTI 220


 >gi|34856013|ref|XP_214939.2| G similar to kallikrein [Rattus norvegicus]
         Length = 275

 Score =  195 bits (496), Expect = 8e-49
 Identities = 91/237 (38%), Positives = 135/237 (56%), Gaps = 15/237 (6%)
```

```
Query: 26   QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
            Q ++V G  C K+S P+Q A+        LCGGVLIDP WV+TAAHC       V+LG+HNL
Sbjct: 38   QSRIVGGYNCEKNSQPWQVAVIN--RYLCGGVLIDPSWVITAAHCYSHYYHVLLGRHNLF 95

Query: 86   QTETFQRQISVDRTIVHPRYNP-----------ETHDNDIMMVHLKNPVKFSKKIQPLPL 134
            + E F +    V ++  HP YNP                + ND+M++HL  P    +  ++ + L
Sbjct: 96   EDEPFAQYRFVSQSFPHPDYNPFLMRNHTRQTGYDYSNDLMLLHLSEPADITDGVKVIDL 155

Query: 135  KNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGD 192
              +   +     C + GWG   +     + PD +QC ++ L+  E+C  AY  K+T  M+CAG
Sbjct: 156  PTEEPKVGSTCLVSGWGSTKPLISELPDDLQCVNIDLLSNEKCIEAYRWKVTDLMLCAGK 215

Query: 193  MKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
            ++ G D+C GDSGGPL+C G L+GL SWG +PC       PG+YT +       WI+ +++
Sbjct: 216  LEGGKDACNGDSGGPLICDGVLQGLTSWGSVPCSEPHNPGIYTKIIKFTSWIKEVMK 272
```

>gi|40647097|gb|AAR88364.1| pretrypsinogen [Tautogolabrus adspersus]
Length = 242

Score = 195 bits (496), Expect = 8e-49
Identities = 93/242 (38%), Positives = 146/242 (60%), Gaps = 4/242 (1%)

```
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M+ L   L++  +A++ + +K+V G  C   S P   +L  SG+  CGG L++  WV++A
Sbjct: 1    MRSLVFVLLIG-AAFAIDDDKIVGGYECTPHSQPHTVSLQ-SGYHFCGGSLVNEDWVVSA 58

Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSK 127
            AHC K  +QV LG+H++R  E  ++ IS  R I HPRY+    DNDIM++ L      ++
Sbjct: 59   AHCYKSRIQVRLGEHHIRVNEGTEQIISSSRVIRHPRYSSYNIDNDIMLIKLSQSATLNQ 118

Query: 128  KIQPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQS 186
             ++ + L    C+     C++ GWG  M +    D +QC ++ ++    C+ +YPG IT +
Sbjct: 119  YVKTVALPTSCAPAGTMCKVAGWGNTMSSSADGDKLQCLNIPILSERDCDNSYPGMITDA 178

Query: 187  MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M CAG ++ G DSCQGDSGGP+VC G+L+G+VSWG    C  ++ PGVY  VC    W+++
Sbjct: 179  MFCAGYLEGGKDSCQGDSGGPVVCNGQLQGVVSWG-YGCAERDHPGVYAKVCLFNDWLES 237

Query: 247  IL 248
             +
Sbjct: 238  TM 239
```

>gi|58257844|gb|AAW69363.1| try10 [Macaca mulatta]
Length = 248

Score = 195 bits (496), Expect = 8e-49
Identities = 95/228 (41%), Positives = 139/228 (60%), Gaps = 5/228 (2%)

```
Query: 24   EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHC-KKPNLQVILGKH 82
            ++ +K+V G  C ++S P+Q +L  SG+  CGG LI  QWV++A HC K   +QV LG+H
Sbjct: 19   DDDDKIVGGYTCEENSVPYQVSL-NSGYHFCGGSLIREQWVVSAGHCWKLGRIQVRLGEH 77

Query: 83   NLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEEN 142
            N+    E  ++ I+  + I HP+YN +T DNDI+++ L  P   +  +   +PL
Sbjct: 78   NIEVLEGNEQFINAAKKIRHPKYNRKTLDNDILLIKLSTPAVINDHVSTIPLPTAPPAAG 137
```

```
Query: 143 PNCQILGWGK--MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSC 200
               I GWG        D+PD +QC D  ++ + +CE +YPGKIT +M C G ++ G DSC
Sbjct: 138 AEALISGWGNTLSSGADYPDELQCLDAPVLSQAECEASYPGKITSNMFCVGFLEGGKDSC 197

Query: 201 QGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           QGDSGGP+V  G L+G+VSWG    C  K KPGVYT V  ++ WI++ +
Sbjct: 198 QGDSGGPVVSNGELQGIVSWG-YGCAQKNKPGVYTKVYNYVDWIEDTI 244
```

>gi|3452117|gb|AAC32751.1| trypsinogen 1 precursor [Pseudopleuronectes americanus]
Length = 250

Score = 195 bits (496), Expect = 8e-49
Identities = 104/248 (41%), Positives = 144/248 (58%), Gaps = 9/248 (3%)

```
Query: 8   MKMLALCLVL-AKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLT 66
           M +LAL L++ A  A    E  +++ G  C    S P+ A+L    G+   CGGVLI+ QWVL+
Sbjct: 1   MNLLALLLMVGAAVAVPREDGRIIGGHECAAHSRPYMASL-NYGYHFCGGVLINNQWVLS 59

Query: 67  AAHC--KKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVK 124
            AHC       +QV+LG+HNLR  E   ++ +   D   I HP Y+ +T D DIM++ L +PV+
Sbjct: 60  VAHCWYNPYAMQVMLGEHNLRVFEGTEQLMKTDTIIWHPNYDYQTLDFDIMLIKLYHPVE 119

Query: 125 FSKKIQPLPLKNDCSEENPNCQILGWGKM-ENGD---FPDTIQCADVHLVPREQCERAYP 180
            ++ + P+ L + C       C + GWG     +GD     P  +QC DV ++   EQC ++YP
Sbjct: 120 VTEAVAPISLPSSCPVGGTPCSVSGWGNTARDGDDVYMPTLLQCMDVPIIDEEQCMKSYP 179

Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
           G I+  MVCAG M    D+C GDSG PLVC G + GLVSWG    C      PGVY  +C
Sbjct: 180 GMISPRMVCAGFMDGSRDACNGDSGSPLVCRGEVTGLVSWG-QGCAQPNYPGVYVKLCEF 238

Query: 241 IRWIQNIL 248
              WI+N L
Sbjct: 239 HAWIENTL 246
```

>gi|609583|gb|AAA58781.1| G kallikrein
Length = 235

Score = 195 bits (496), Expect = 8e-49
Identities = 91/234 (38%), Positives = 134/234 (57%), Gaps = 15/234 (6%)

```
Query: 29  VVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQTE 88
           +V G  C K+S P+Q A+        LCGGVLIDP WV+TAAHC        V+LG+HNL + E
Sbjct: 1   IVGGYKCEKNSQPWQVAVIN--RYLCGGVLIDPSWVITAAHCYSHYYHVLLGRHNLFEDE 58

Query: 89  TFQRQISVDRTIVHPRYNP-----------ETHDNDIMMVHLKNPVKFSKKIQPLPLKND 137
            F +    V ++   HP YNP                + ND+M++HL   P    +  ++ + L  +
Sbjct: 59  PFAQYRFVSQSFPHPDYNPFLMRNHTRQTGYDYSNDLMLLHLSEPADITDGVKVIDLPTE 118

Query: 138 CSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKE 195
            +      C + GWG  +      + PD +QC ++ L+   E+C  AY  K+T  M+CAG ++
Sbjct: 119 EPKVGSTCLVSGWGSTKPLISELPDDLQCVNIDLLSNEKCIEAYRWKVTDLMLCAGKLEG 178

Query: 196 GNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
           G D+C GDSGGPL+C G L+GL SWG +PCG     PG+YT +      WI+ +++
```

```
Sbjct: 179 GKDACNGDSGGPLICDGVLQGLTSWGSVPCGEPHNPGIYTKIIKFTSWIKEVMK 232
```

>gi|1334753|emb|CAA54215.1| trypsinogen X [Gadus morhua]
Length = 240

```
 Score =  195 bits (495), Expect = 1e-48
 Identities = 96/238 (40%), Positives = 141/238 (59%), Gaps = 3/238 (1%)

Query: 12  ALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCK 71
            +L  VL   A    E++K+V G  C + S   Q +L  SG+  CGG L+   WV++AAHC
Sbjct: 2   SLIFVLLLGAVFAEEDKIVGGYECTRHSQAHQVSL-NSGYHFCGGSLVSKDWVVSAAHCY 60

Query: 72  KPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQP 131
            K  L+V LG+H++R  E  ++ IS    I HP Y+     DNDIM++ L  P   ++ +
Sbjct: 61  KSVLRVRLGEHHIRVNEGTEQFISSSSVIRHPNYSSYNIDNDIMLIKLTEPATLNQYVHA 120

Query: 132 LPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCA 190
            + L  +C+ +   C + GWG  M + D  D +QC ++ ++    C  +YPG ITQSM CA
Sbjct: 121 VALPTECAADATMCTVSGWGNTMSSVDDGDKLQCLNLPILSHADCANSYPGMITQSMFCA 180

Query: 191 GDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            G ++ G DSCQGDSGGP+VC G L+G+VSWG   C  ++ PGVY  VC   W+++ +
Sbjct: 181 GYLEGGKDSCQGDSGGPVVCNGVLQGVVSWG-YGCAERDNPGVYAKVCVLSGWVRDTM 237
```

>gi|58257848|gb|AAW69367.1| try16 [Macaca mulatta]
Length = 247

```
 Score =  195 bits (495), Expect = 1e-48
 Identities = 96/242 (39%), Positives = 150/242 (61%), Gaps = 5/242 (2%)

Query: 10  MLALCLV-LAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            +L L  V +A +A  ++ +K+V G  C ++S P+Q +L  SG+  CGG LI+ QWV++AA
Sbjct: 4   LLILAFVGVAVAAPFDDDDKIVGGYTCEENSVPYQVSL-NSGYHFCGGSLINEQWVVSAA 62

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  +QV LG+HN+  E  ++ I+  + I HP Y+ +T +NDI+++ L +P   + +
Sbjct: 63  HCYKTRIQVRLGEHNIEVLEGTEQFINAAKIIRHPDYDRKTLNNDILLIKLSSPAVINAR 122

Query: 129 IQPLPLKNDCSEENPNCQILGWGKM--ENGDFPDTIQCADVHLVPREQCERAYPGKITQS 186
            +  + L              I GWG        D+PD +QC +  ++ + +CE +YPGKIT +
Sbjct: 123 VSTISLPTAPPAAGAEALISGWGNTLSSGADYPDELQCLEAPVLSQAECEASYPGKITSN 182

Query: 187 MVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
            M C G ++ G DSCQGDSGGP+V  G+L+G+VSWG   C  K +PGVYT V  ++ WI++
Sbjct: 183 MFCVGFLEGGKDSCQGDSGGPVVSNGQLQGIVSWG-YGCAQKNRPGVYTKVYNYVDWIRD 241

Query: 247 IL 248
             +
Sbjct: 242 TI 243
```

>gi|476825|pir||A44284   tissue kallikrein (EC 3.4.21.35) homolog - rat (fragment)
gi|259431|gb|AAB24071.1| G T-kininogenase [Rattus sp.]

gi|547792|sp|P36375|KLK10_RAT Glandular kallikrein 10 precursor (Tissue kallikrein (T-kininogenase) (K10) (Proteinase B) (Endopeptidase K)
Length = 244

```
 Score =  195 bits (495), Expect = 1e-48
 Identities = 91/237 (38%), Positives = 138/237 (58%), Gaps = 15/237 (6%)

Query: 26   QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
            Q ++V G  C K+S P+Q A+       LCGGVLIDP WV+TAAHC        V+LG++NL
Sbjct: 7    QSRIVGGYKCEKNSQPWQVAIINE--YLCGGVLIDPSWVITAAHCYSNYYHVLLGRNNLF 64

Query: 86   QTETFQRQISVDRTIVHPRYNP-----------ETHDNDIMMVHLKNPVKFSKKIQPLPL 134
            + E F +    V+++   HP Y P            + + ND+M++HL   P    +  ++ + L
Sbjct: 65   EDEPFAQYRFVNQSFPHPDYKPFLMRNHTRQRGDDYSNDLMLLHLSEPADITDGVKVIDL 124

Query: 135  KNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGD 192
              +  +    C    GWG   +  N  +  PD  +QC  ++HL+  E+C  AY  K+T  M+CAG+
Sbjct: 125  PTEEPKVGSTCLASGWGSTKPLNWELPDDLQCVNIHLLSNEKCIEAYEQKVTDLMLCAGE 184

Query: 193  MKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
            M     D+C+GDSGGPL+C  G L+G+  SWG++PC        PGVYT +     WI+ +++
Sbjct: 185  MDGRKDTCKGDSGGPLICDGVLQGITSWGNVPCAEPYNPGVYTKLIKFTSWIKEVMK 241
```

>gi|2507250|sp|P16049|TRY1_GADMO   Trypsin I precursor
Length = 241

```
 Score =  194 bits (493), Expect = 2e-48
 Identities = 97/242 (40%), Positives = 141/242 (58%), Gaps = 3/242 (1%)

Query: 10   MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            M +L  VL   A   E++K+V G  C K S   Q +L  SG+  CGG L+   WV++AAH
Sbjct: 1    MKSLIFVLLLGAVFAEEDKIVGGYECTKHSQAHQVSL-NSGYHFCGGSLVSKDWVVSAAH 59

Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C K  L+V LG+H++R  E  ++ IS   I HP Y+   +NDIM++ L  P   ++ +
Sbjct: 60   CYKSVLRVRLGEHHIRVNEGTEQYISSSSVIRHPNYSSYNINNDIMLIKLTKPATLNQYV 119

Query: 130  QPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMV 188
              + L  +C+ +  C + GWG  M +   D +QC  + ++   C  +YPG ITQSM
Sbjct: 120  HAVALPTECAADATMCTVSGWGNTMSSVADGDKLQCLSLPILSHADCANSYPGMITQSMF 179

Query: 189  CAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
            CAG ++ G DSCQGDSGGP+VC G L+G+VSWG  C  ++ PGVY  VC   W+++ +
Sbjct: 180  CAGYLEGGKDSCQGDSGGPVVCNGVLQGVVSWG-YGCAERDHPGVYAKVCVLSGWVRDTM 238

Query: 249  RN 250
             N
Sbjct: 239  AN 240
```

>gi|57037489|ref|XP_541469.1| PREDICTED: similar to kallikrein 5 preproprotein [(
Length = 464

```
 Score =  194 bits (493), Expect = 2e-48
 Identities = 91/248 (36%), Positives = 148/248 (59%), Gaps = 26/248 (10%)
```

```
Query: 28   KVVHGGPCLKDSHPFQAALYTSGH-LLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQ 86
            ++V+G  C K++ P+Q AL     + L CG VL++PQW+LTAAHC+KP  ++ LG H+L
Sbjct: 216  RIVNGTDCEKNAQPWQGALLLGPNKLYCGAVLVNPQWLLTAAHCRKPFFRIRLGHHSLSP 275

Query: 87   T-ETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENPNC 145
              E  Q+      ++I HP Y+    H ND+M++ L    ++ +++++P+ + + C     +C
Sbjct: 276  VYEAGQQLFKGIKSIPHPGYSHPGHSNDLMLIKLNRKIRETQRVKPINISSKCPSAGTSC 335

Query: 146  QILGWGKMENGD-----------FPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMK 194
             + GWG   + +             FP  +QC ++ ++   ++C +AYP +I  +M CAGD +
Sbjct: 336  MVSGWGTTNSPNVALLCVFLTVQFPKVLQCLNITVLSDDRCRKAYPRQIDSTMFCAGD-E 394

Query: 195  EGNDSCQ------------GDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIR 242
             G DSCQ            GDSGGP+VC G L+GLVSWGD PC     +PGVYT++C    +
Sbjct: 395  AGRDSCQTSSGFSYQFVVRGDSGGPVVCNGSLQGLVSWGDFPCAQPNRPGVYTNLCQFTK 454

Query: 243  WIQNILRN 250
            WI++ +++
Sbjct: 455  WIKDTIQS 462
```

>gi|33307101|gb|AAQ02911.1| serine protease KN13 precursor [Trimeresurus stejneger:
Length = 258

```
 Score =  194 bits (493), Expect = 2e-48
 Identities = 99/248 (39%), Positives = 143/248 (57%), Gaps = 4/248 (1%)

Query: 5    MLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M+ +++LA  L+L  S       E V+ G  C  + H F  ALY SG   CGG LI+ +WV
Sbjct: 1    MVLIRVLANLLILQLSYAQRSSELVIGGDECNINEHRFLVALYKSGRFRCGGTLINQEWV 60

Query: 65   LTAAHCKKPNLQVILGKHNLR-QTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPV 123
            LTAAHC + N+++ LG H+     E  QR++  ++         N    + DIM++ L +PV
Sbjct: 61   LTAAHCDRRNMEIKLGMHSKNVPNEDEQRRVPKEKFFCDSNKNHTQWNKDIMLIRLNSPV 120

Query: 124  KFSKKIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLVPREQCERAYPG 181
              S  I PL L ++         C+I+GWG +   N  +PD   CA+++L       C  A+ G
Sbjct: 121  NNSTHIAPLSLPSNPPIVGSVCRIMGWGTITSPNETYPDVPHCANINLFNYTVCHGAHAG 180

Query: 182  -KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
              T    +CAG ++EG D+C+GDSGGPL+C G+ +G+VSWG  PC    +PGVYT V  H
Sbjct: 181  LPATSRTLCAGVLEEGKDTCKGDSGGPLICNGQFQGIVSWGGDPCAQPREPGVYTKVFDH 240

Query: 241  IRWIQNIL 248
            + WIQNI+
Sbjct: 241  LDWIQNII 248
```

>gi|33637113|gb|AAQ23713.1| glandular kallikrein precursor [Equus caballus]
Length = 261

```
 Score =  194 bits (492), Expect = 2e-48
 Identities = 96/257 (37%), Positives = 144/257 (56%), Gaps = 16/257 (6%)

Query: 8    MKMLALCLVLA---KSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M +  LCL L+      A     Q +++ G  C   S P+QAA+Y       CGGVL+DPQWV
Sbjct: 1    MWLPVLCLALSLVGTGAAPPIQSRIIGGWECKNHSKPWQAAVYHYSSFQCGGVLVDPQWV 60
```

```
Query: 65   LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP-----------ETHDND 113
            LTAAHCK     Q+ LG+HNL + E     +    V ++   HP +N            E + +D
Sbjct: 61   LTAAHCKGDYYQIWLGRHNLFEDEDTAQFFLVAKSFPHPDFNMSLLENNNRLPGEDYSHD 120

Query: 114  IMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVP 171
            +M++  ++  P + +   +Q L L             C    GWG +E     F   PD ++C D+ L+
Sbjct: 121  LMLLQVEQPDQITVAVQVLALPTQEPVLGSTCYASGWGSIEPDKFTYPDELRCVDLTLLS 180

Query: 172  REQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKP 231
             + C+ A+     +T+ M+CAG ++ G D+C GDSGGPL+C G  +G+ SWG +PCG   KP
Sbjct: 181  NDVCDNAHSQNVTEYMLCAGHLEGGKDTCVGDSGGPLICDGVFQGVTSWGHIPCGRPNKP 240

Query: 232  GVYTDVCTHIRWIQNIL 248
             VYT +   H++WIQ+ +
Sbjct: 241  AVYTKLIPHVQWIQDTI 257
```

>gi|1334752|emb|CAA54214.1| trypsinogen I [Gadus morhua]
gi|481640|pir||S39047 trypsin (EC 3.4.21.4) I - Atlantic cod
Length = 240

```
 Score =  193 bits (490), Expect = 4e-48
 Identities = 96/240 (40%), Positives = 140/240 (58%), Gaps = 3/240 (1%)

Query: 12   ALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCK 71
            +L  VL   A   E++K+V G  C K S    Q +L  SG+  CGG L+    WV++AAHC
Sbjct: 2    SLIFVLLLGAVFAEEDKIVGGYECTKHSQAHQVSL-NSGYHFCGGSLVSKDWVVSAAHCY 60

Query: 72   KPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQP 131
            K  L+V LG+H++R   E   ++ IS     I HP Y+     +NDIM++ L   P    ++ +
Sbjct: 61   KSVLRVRLGEHHIRVNEGTEQYISSSSVIRHPNYSSYNINNDIMLIKLTKPATLNQYVHA 120

Query: 132  LPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCA 190
            + L   +C+ +    C + GWG  M +      D +QC  + ++    C  +YPG ITQSM CA
Sbjct: 121  VALPTECAADATMCTVSGWGNTMSSVADGDKLQCLSLPILSHADCANSYPGMITQSMFCA 180

Query: 191  GDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
            G ++ G DSCQGDSGGP+VC G L+G+VSWG    C   ++ PGVY  VC    W+++ + N
Sbjct: 181  GYLEGGKDSCQGDSGGPVVCNGVLQGVVSWG-YGCAERDHPGVYAKVCVLSGWVRDTMAN 239
```

>gi|64382|emb|CAA49676.1| trypsin IA [Salmo salar]
gi|422582|pir||S31776 trypsin (EC 3.4.21.4) IA precursor - Atlantic salmon
Length = 242

```
 Score =  193 bits (490), Expect = 4e-48
 Identities = 96/241 (39%), Positives = 141/241 (58%), Gaps = 4/241 (1%)

Query: 10   MLALCLVLA-KSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            M++L   VL    +A++ E +K+V G   C    S    Q +L  SG+  CGG L++   WV++AA
Sbjct: 1    MISLVFVLLIGAAFATEDDKIVGGYECKAYSQAHQVSL-NSGYHFCGGSLVNENWVVSAA 59

Query: 69   HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K   ++V LG+HN++ TE   ++ IS  R I HP Y+    DNDIM++ L   P    +
Sbjct: 60   HCYKSRVEVRLGEHNIKVTEGSEQFISSSRVIRHPNYSSYNIDNDIMLIKLSKPATLNTY 119
```

```
Query: 129 IQPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 187
           +QP+ L   C+     C + GWG  M +    + +QC ++ ++    C  +YPG IT +M
Sbjct: 120 VQPVALPTSCAPAGTMCTVSGWGNTMSSTADSNKLQCLNIPILSYSDCNNSYPGMITNAM 179

Query: 188 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
            CAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C     PGVY  VC    W+ +
Sbjct: 180 FCAGYLEGGKDSCQGDSGGPVVCNGELQGVVSWG-YGCAEPGNPGVYAKVCIFNDWLTST 238

Query: 248 L 248
           +
Sbjct: 239 M 239
```

>gi|64380|emb|CAA49680.1| trypsin I [Salmo salar]
gi|422581|pir||S31775 trypsin (EC 3.4.21.4) I precursor - Atlantic salmon
gi|464944|sp|P35031|TRY1_SALSA Trypsin I precursor
Length = 242

Score = 193 bits (490), Expect = 4e-48
Identities = 96/241 (39%), Positives = 141/241 (58%), Gaps = 4/241 (1%)

```
Query: 10  MLALCLVLA-KSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            M++L  VL   +A++ E +K+V G  C   S   Q +L  SG+  CGG L++  WV++AA
Sbjct: 1   MISLVFVLLIGAAFATEDDKIVGGYECKAYSQTHQVSL-NSGYHFCGGSLVNENWVVSAA 59

Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKK 128
            HC K  ++V LG+HN++ TE  ++ IS  R I HP Y+    DNDIM++ L  P   +
Sbjct: 60  HCYKSRVEVRLGEHNIKVTEGSEQFISSSRVIRHPNYSSYNIDNDIMLIKLSKPATLNTY 119

Query: 129 IQPLPLKNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSM 187
            +QP+ L   C+     C + GWG  M +    + +QC ++ ++    C  +YPG IT +M
Sbjct: 120 VQPVALPTSCAPAGTMCTVSGWGNTMSSTADSNKLQCLNIPILSYSDCNNSYPGMITNAM 179

Query: 188 VCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNI 247
             CAG ++ G DSCQGDSGGP+VC G L+G+VSWG   C     PGVY  VC    W+ +
Sbjct: 180 FCAGYLEGGKDSCQGDSGGPVVCNGELQGVVSWG-YGCAEPGNPGVYAKVCIFNDWLTST 238

Query: 248 L 248
            +
Sbjct: 239 M 239
```

>gi|27731317|ref|XP_218647.1| similar to Kallikrein 9 precursor (Kallikrein-like (KLK-L3) [Rattus norvegicus]
Length = 252

Score = 193 bits (490), Expect = 4e-48
Identities = 96/223 (43%), Positives = 133/223 (59%), Gaps = 8/223 (3%)

```
Query: 28  KVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLRQT 87
            + V    C ++S P+QA L+     LCG  LI+ QW+LTAAHC+KP L V LG+H+L Q
Sbjct: 22  RAVGARECQRNSQPWQAGLFYLTRQLCGATLINDQWLLTAAHCRKPYLWVRLGEHHLWQW 81

Query: 88  ETFQRQISVDRTIVHPRYNPET----HDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEENP 143
            E  ++ + V     HP +NP+     H++DIM++ L   V+ S  +QPL L
Sbjct: 82  EGPEKLLLVTDFFPHPGFNPDLSANDHNDDIMLIRLPRKVRLSPAVQPLNLSQSLPSVGT 141
```

```
Query: 144 NCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDSCQGD 203
            C I GWG       FP T+QCA++ ++   + C  AYPG I++ M+CAG   + G  SCQGD
Sbjct: 142 QCLISGWGIQ----FPMTLQCANISILDNKLCRWAYPGHISEKMLCAGLWEGGRGSCQGD 197

Query: 204 SGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQN 246
           SGGPLVC G L G+VS G   PC     ++P VYT V   ++ WI+N
Sbjct: 198 SGGPLVCKGTLAGIVSGGSEPCSRPQRPAVYTSVFHYLDWIEN 240
```

>gi|52851385|ref|NP_001005382.1| G glandular kallikrein 12, submandibular/renal [Ra
gi|205004|gb|AAA51640.1| G kallikrein precursor RSKG3 [Rattus norvegicus]
gi|92888|pir||B31136 tissue kallikrein (EC 3.4.21.35) 3 precursor, submandibular - r
gi|547793|sp|P36376|KLK12_RAT G Glandular kallikrein 12, submandibular/renal precurs
kallikrein) (RSKG-3)
Length = 259

Score = 193 bits (490), Expect = 4e-48
Identities = 88/237 (37%), Positives = 139/237 (58%), Gaps = 15/237 (6%)

```
Query: 26  QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
           Q +VV G  C K+S P+Q A+       LCGGVLIDP WV+TAAHC    N  V+LG++NL
Sbjct: 22  QSRVVGGYKCEKNSQPWQVAVIN--RYLCGGVLIDPSWVITAAHCYSHNYHVLLGRNNLF 79

Query: 86  QTETFQRQISVDRTIVHPRYNP-----------ETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           + E F +    V+++  HP YNP             + H ND+M++HL   P   +  ++ + L
Sbjct: 80  KDEPFAQYRVVNQSFPHPDYNPFFMKNHTLFPGDDHSNDLMLLHLSEPADITDGVKVIDL 139

Query: 135 KNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGD 192
             +  +    C   GW    +      +FPD +QC +++++  E+C +A++    +T  M+CAG+
Sbjct: 140 PTEEPKVGSTCLASGWSSTKPLEWEFPDDLQCVNINILSNEKCIKAHTQMVTDVMLCAGE 199

Query: 193 MKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
           ++ G D+C GDSGGPL+C G L+G+ SW +PCG    +P +YT +     WI+ +++
Sbjct: 200 LEGGKDTCNGDSGGPLLCDGVLQGITSWSSVPCGETNRPAIYTKLIKFTSWIKEVMK 256
```

>gi|64386|emb|CAA49678.1| trypsin II [Salmo salar]
gi|422584|pir||S31778 trypsin (EC 3.4.21.4) II precursor - Atlantic salmon (fragmen
gi|464946|sp|P35032|TRY2_SALSA Trypsin II precursor
Length = 231

Score = 192 bits (489), Expect = 5e-48
Identities = 92/230 (40%), Positives = 136/230 (59%), Gaps = 3/230 (1%)

```
Query: 20  SAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVIL 79
           +A++ E +K+V G  C    S P Q +L  SG+  CGG L++  WV++AAHC +  ++V L
Sbjct: 1   AAFATEDDKIVGGYECKAYSQPHQVSL-NSGYHFCGGSLVNENWVVSAAHCYQSRVEVRL 59

Query: 80  GKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCS 139
           G+HN++ TE   ++ IS   R I HP Y+     DNDIM++ L   P    +  +QP+ L   C+
Sbjct: 60  GEHNIQVTEGSEQFISSSRVIRHPNYSSYNIDNDIMLIKLSKPATLNTYVQPVALPTSCA 119

Query: 140 EENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGND 198
                C + GWG  M +     + +QC ++ ++     C   +YPG IT +M CAG ++ G D
Sbjct: 120 PAGTMCTVSGWGNTMSSTADKNKLQCLNIPILSYSDCNNSYPGMITNAMFCAGYLEGGKD 179

Query: 199 SCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
```

```
         SCQGDSGGP+VC G L+G+VSWG   C     PGVY  VC    W+ + +
Sbjct: 180 SCQGDSGGPVVCNGELQGVVSWG-YGCAEPGNPGVYAKVCIFNDWLTSTM 228
```

>gi|51591907|ref|NP_001003977.1| glandular kallikrein 11 [Rattus norvegicus]
gi|47169500|tpe|CAE48387.1| TPA: glandular kallikrein-11 [Rattus norvegicus]
Length = 257

Score = 192 bits (489), Expect = 5e-48
Identities = 92/237 (38%), Positives = 139/237 (58%), Gaps = 17/237 (7%)

```
Query: 26  QEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNLR 85
           Q +VV G  C K+S P+Q A+ +     LCGGVLIDP WV+TAAHC    +  V+LG++NL
Sbjct: 22  QSRVVGGYKCEKNSQPWQVAVISRS--LCGGVLIDPSWVITAAHCY--SYHVLLGRNNLS 77

Query: 86  QTETFQRQISVDRTIVHPRYNP-----------ETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           + E F +    V ++  HP YNP            + + ND+M++HL  P    +  ++ + L
Sbjct: 78  EDEPFAQYRFVSQSFPHPDYNPFFMRNHTRQPGDDYSNDLMLLHLSKPADITDGVKVIDL 137

Query: 135 KNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPGKITQSMVCAGD 192
            +  +     C    GWG  + D+   PD +QC ++HL+  E+C  AY  K+T  M+CAGD
Sbjct: 138 PTEEPKVGSTCLASGWGSTKPLDWELPDDLQCVNIHLLSNEKCIEAYNEKVTDLMLCAGD 197

Query: 193 MKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILR 249
           ++ G D+C+GDSGGPL+C G L+G+ SWG  PC      P +YT +      WI+ +++
Sbjct: 198 LEGGKDTCKGDSGGPLICDGVLQGITSWGSDPCAEPNMPAIYTKLIKFTSWIKEVMK 254
```

>gi|809221|pdb|1BIT| The Crystal Structure Of Anionic Salmon Trypsin In A Seconc
Form
Length = 237

Score = 192 bits (489), Expect = 5e-48
Identities = 93/235 (39%), Positives = 138/235 (58%), Gaps = 3/235 (1%)

```
Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPN 74
           ++L  +A++ E +K+V G  C   S  Q +L  SG+  CGG L++  WV++AAHC K
Sbjct: 2   VLLIGAAFATEDDKIVGGYECKAYSQAHQVSL-NSGYHFCGGSLVNENWVVSAAHCYKSR 60

Query: 75  LQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPLPL 134
           ++V LG+HN++ TE  ++ IS  R I HP Y+    DNDIM++ L  P   +  +QP+ L
Sbjct: 61  VEVRLGEHNIKVTEGSEQFISSSRVIRHPNYSSYNIDNDIMLIKLSKPATLNTYVQPVAL 120

Query: 135 KNDCSEENPNCQILGWGK-MENGDFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDM 193
              C+     C + GWG  M +     + +QC ++ ++    C  +YPG IT +M CAG +
Sbjct: 121 PTSCAPAGTMCTVSGWGNTMSSTADSNKLQCLNIPILSYSDCNNSYPGMITNAMFCAGYL 180

Query: 194 KEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNIL 248
           + G DSCQGDSGGP+VC G L+G+VSWG   C     PGVY  VC    W+ + +
Sbjct: 181 EGGKDSCQGDSGGPVVCNGELQGVVSWG-YGCAEPGNPGVYAKVCIFNDWLTSTM 234
```

>gi|67558|pir||KQHU tissue kallikrein (EC 3.4.21.35) precursor [validated] - human
gi|125170|sp|P06870|KLK1_HUMAN Kallikrein 1 precursor (Tissue kallikrein)
(Kidney/pancreas/salivary gland kallikrein)

```
gi|186653|gb|AAA36136.1|  G  kallikrein
         Length = 262

 Score =  192 bits (488), Expect = 7e-48
 Identities = 97/258 (37%), Positives = 145/258 (56%), Gaps = 17/258 (6%)

Query: 8   MKMLALCLVLA---KSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M  L LCL L+      A     Q ++V G   C + S P+QAALY       CGG+L+   QWV
Sbjct: 1   MWFLVLCLALSLGGTGAAPPIQSRIVGGWECEQHSQPWQAALYHFSTFQCGGILVHRQWV 60

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN-----------PETHDND 113
            LTAAHC    N Q+ LG+HNL    E     + + V   +   HP +N                E + +D
Sbjct: 61  LTAAHCISDNYQLWLGRHNLFDDENTAQFVHVSESFPHPGFNMSLLENHTRQADEDYSHD 120

Query: 114 IMMVHLKNPVK-FSKKIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLV 170
            +M++ L   P     +   ++ + L       E     C     GWG +E   N    FPD +QC D+ ++
Sbjct: 121 LMLLRLTEPADTITDAVKVVELPTQEPEVGSTCLASGWGSIEPENFSFPDDLQCVDLKIL 180

Query: 171 PREQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEK 230
            P ++CE+A++    K+T    M+C G ++ G D+C GDSGGPL+C G L+G+ SWG +PCG+    K
Sbjct: 181 PNDECEKAHVQKVTDFMLCVGHLEGGKDTCVGDSGGPLMCDGVLQGVTSWGYVPCGTPNK 240

Query: 231 PGVYTDVCTHIRWIQNIL 248
            P V    V ++++WI++ +
Sbjct: 241 PSVAVRVLSYVKWIEDTI 258


>gi|31980868|ref|NP_034769.4|  G  kallikrein 6 [Mus musculus]
 gi|20379615|gb|AAH27736.1|  G  Kallikrein 6 [Mus musculus]
 gi|14789646|gb|AAH10754.1|  G  Kallikrein 6 [Mus musculus]
 gi|31657181|gb|AAH53697.1|  G  Kallikrein 6 [Mus musculus]
 gi|17433705|sp|P15947|KLK6_MOUSE  G  Glandular kallikrein K6 precursor (Tissue kallikr
          (Renal kallikrein) (KAL-B)
 gi|520591|dbj|BAA01257.1|  G  tissue kallikrein [Mus musculus]
 gi|12832144|dbj|BAB21982.1|  G  unnamed protein product [Mus musculus]
         Length = 261

 Score =  192 bits (487), Expect = 9e-48
 Identities = 98/257 (38%), Positives = 141/257 (54%), Gaps = 16/257 (6%)

Query: 8   MKMLALCLVLAKS---AWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWV 64
            M+ L L L L+      A     Q ++V G    C K+S P+Q A+Y       CGG+L++   WV
Sbjct: 1   MRFLILFLALSLGGIDAAPPVQSRIVGGFNCEKNSQPWQVAVYRFTKYQCGGILLNANWV 60

Query: 65  LTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYN--------PETHD---ND 113
            LTAAHC      QV LGK+N  + E     +     V + I HP +N          P+  D    ND
Sbjct: 61  LTAAHCHNDKYQVWLGKNNFLEDEPSAQHRLVSKAIPHPDFNMSLLNEHTPQPEDDYSND 120

Query: 114 IMMVHLKNPVKFSKKIQPLPLKNDCSEENPNCQILGWGKME--NGDFPDTIQCADVHLVP 171
            +M++ LK P   +  ++P+ L  +  +    C     GWG +    ++PD +QC ++ L+P
Sbjct: 121 LMLLRLKKPADITDVVKPIDLPTEEPKLGSTCLASGWGSITPVKYEYPDELQCVNLKLLP 180

Query: 172 REQCERAYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKP 231
             E C +A+   K+T   M+CAGDM   G D+C GDSGGPL+C G L+G+ SWG  PCG    P
Sbjct: 181 NEDCAKAHIEKVTDDMLCAGDMDGGKDTCAGDSGGPLICDGVLQGITSWGPSPCGKPNVP 240
```

```
Query: 232 GVYTDVCTHIRWIQNIL 248
           G+YT V     WI+  +
Sbjct: 241 GIYTRVLNFNTWIRETM 257
```

Get selected sequences | Select all | Deselect all

```
  Database: All non-redundant GenBank CDS
  translations+PDB+SwissProt+PIR+PRF excluding environmental samples
    Posted date:  Mar 13, 2005  9:25 AM
  Number of letters in database: 802,641,970
  Number of sequences in database:  2,366,628

Lambda     K      H
   0.320    0.137    0.451

Gapped
Lambda     K      H
   0.267   0.0410    0.140


Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Hits to DB: 92,770,297
Number of Sequences: 2366628
Number of extensions: 4131687
Number of successful extensions: 9988
Number of sequences better than 10.0: 906
Number of HSP's better than 10.0 without gapping: 779
Number of HSP's successfully gapped in prelim test: 127
Number of HSP's that attempted gapping in prelim test: 6964
Number of HSP's gapped (non-prelim): 977
length of query: 253
length of database: 802,641,970
effective HSP length: 124
effective length of query: 129
effective length of database: 509,180,098
effective search space: 65684232642
effective search space used: 65684232642
T: 11
A: 40
X1: 16 ( 7.4 bits)
X2: 38 (14.6 bits)
X3: 64 (24.7 bits)
S1: 41 (21.8 bits)
S2: 73 (32.7 bits)
```

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ARTICLE

Human TIMP-3 Is Expressed During Fetal Development, Hair Growth Cycle, and Cancer Progression

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SUMMARY We studied the expression and regulation of TIMP-3, a recently cloned member of the tissue inhibitor of the metalloproteinase family, during human fetal development and in various human tissues, with emphasis on epithelial structures. Expression of TIMP-3 mRNA was detected by in situ hybridization in developing bone, kidney, and various mesenchymal structures. At 16 weeks of gestation, ectoderm-derived cells of hair germs expressed TIMP-3 mRNA, and beginning from the twentieth week consistent expression was detected in epithelial outer root sheath cells of growing hair follicles. In normal adult human skin, expression of TIMP-3 mRNA was limited to hair follicles, starting at the early anagen (growing) phase and vanishing at the catagen (regressing) phase. TIMP-3 mRNA was not detected in benign hair follicle-derived tumors but was present in tumor cells of infiltrative basal cell carcinomas and in surrounding stromal cells in squamous cell carcinomas. Human primary keratinocytes in culture expressed TIMP-3 mRNAs, the levels of which were upregulated by transforming growth factor-β (TGF-β), whereas interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) had no effect. Our results suggest a role for TIMP-3 in connective tissue remodeling during fetal development, hair growth cycle, and cancer progression. (J Histochem Cytochem 46:437–447, 1998)

KEY WORDS
carcinogenesis
extracellular matrix
hair
TGF-β

THE MATRIX metalloproteinases (MMPs, matrixins) are a family of structurally related neutral proteinases involved in the remodeling of extracellular matrix (ECM) in processes such as fetal development, wound healing, inflammation, and tumor invasion (Birkedal-Hansen 1995). These enzymes have overlapping specificities, being able to degrade important ECM macromolecules such as different types of collagens, laminin, proteoglycans, elastin, and fibronectin (Woessner 1991). The activity of metalloproteinases is regulated at several levels, including gene transcription, activation of secreted proenzymes, and inhibition by a class of natural inhibitors called TIMPs (tissue inhibitors of metalloproteinases). TIMPs are secreted proteins that inhibit MMPs by binding to their active site in a 1:1 stoichiometric ratio. Recently, two new members of the TIMP family have been cloned: TIMP-3 (Apte et al. 1994b; Silbiger et al. 1994; Uria et al. 1994) and TIMP-4 (Greene et al. 1996; Leco et al. 1997). TIMP-3 shares an identity of 39% to TIMP-1, 46% to TIMP-2, and 45% to TIMP-4 in amino acid sequence (Silbiger et al. 1994; Leco et al. 1997), and inhibits interstitial collagenase (MMP-1), collagenase-3 (MMP-13), stromelysin-1 (MMP-3), 72-kD and 92-kD gelatinases (MMP-2 and -9), and membrane Type 1 MMP (MMP-14) (Apte et al. 1995; Knäuper et al. 1996; Will et al. 1996). Instead of being soluble like TIMP-1 and -2, it is tightly bound to the extracellular matrix and has a distinctive pattern of expression compared to the other TIMPs (Leco et al. 1994).

TIMP-3 mRNA was first detected in human breast tumors (Uria et al. 1994), in metastatic melanoma cell

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lines (Silbiger et al. 1994), and in various normal adult tissues such as placenta, kidney, heart, prostate, small intestine, and lung, and in fetal tissues including heart, lung, and kidney by Northern blot hybridization (Apte et al. 1994b; Wick et al. 1994; Wilde et al. 1994). With in situ hybridization, expression of murine TIMP-3 mRNA has been reported during mouse embryo implantation (Harvey et al. 1995; Reponen et al. 1995; Alexander et al. 1996; Leco et al. 1996) and in developing kidney, cartilage, and various epithelial structures, including epidermis and intestinal mucosa (Apte et al. 1994a). Little is known, however, about the role of TIMP-3 in human tissues in vivo, because expression of TIMP-3 mRNA has only been localized to cells of early placental structures (Byrne et al. 1995; Higuchi et al. 1995; Hurskainen et al. 1996), fetal retinal epithelium (Ruiz et al. 1996), and fibroblastic cells within breast cancer stroma (Byrne et al. 1995). Furthermore, TIMP-3 protein has been found to be an extracellular matrix component of Bruch's membrane of the human eye (Fariss et al. 1997).

TIMP-3 is induced in response to mitogenic stimulation and is regulated during normal cell cycle progression (Wick et al. 1994). A potential role for TIMP-3 in carcinogenesis has been proposed. Chicken TIMP-3 promotes oncogenic transformation in cultured cells (Yang and Hawkes 1992), and TIMP-3 overexpression inhibits human colon carcinoma growth in vivo (Bian et al. 1996). A direct implication for a human disease is the presence of point mutations in the TIMP-3 gene in patients with Sorsby's fundic dystrophy, an autosomal dominant disorder leading to visual loss (Weber et al. 1994).

To explore the physiological role of TIMP-3 in human tissues, we have determined its spatial and temporal expression during fetal development. We have also examined its expression in adult skin and various organs of the body, with special emphasis on epithelial components based on previous data on mouse tissues (Apte et al. 1994a). We report here that in early human fetus TIMP-3 is expressed in cartilage, bone, kidney, and in mesenchymal cells within the connective tissue. At 16 weeks of gestation, ectoderm-derived cells of hair germs express TIMP-3 mRNA, and beginning from the twentieth week consistent expression is detected in epithelial outer root sheath cells of growing hair follicles. In fully developed follicles, expression of TIMP-3 mRNA is cyclic, starting at the early anagen (growing) phase and vanishing at the catagen (regressing) phase. TIMP-3 mRNA is not detected in benign hair follicle-derived tumors but is present in tumor cells of infiltrative basal cell carcinomas and in surrounding stromal cells in squamous cell carcinomas. In vitro TIMP-3 gene expression in primary human epidermal keratinocytes is induced by TGF-β, but not by IL-1β or TNF-α. Our results substantiate the role of TIMP-3 in development, hair growth cycle, and tumor growth.

Materials and Methods

Tissues

Formalin-fixed, paraffin-embedded specimens were obtained from the Departments of Dermatology and Pathology, University of Helsinki, Finland. All fetal material originated from medical abortions and was obtained from the Department of Pathology, University of Oulu, Finland. Fetal age was estimated by menstrual age and histological examination. This study was approved by the ethics committee of the Department of Dermatology, Helsinki, Finland. The following subgroups of histological sections were examined.

1. Fetal tissues: complete fetus at gestational age of 7, 8–9, 10, and 12 weeks and biopsies of the scalp and trunk skin at gestational age of 16, 20, 21, and 23 weeks.
2. Adult skin specimens: basal cell carcinoma $n = 8$ (infiltrative $n = 5$, keratotic $n = 3$), squamous cell carcinoma $n = 5$, trichofolliculoma $n = 4$, trichoepithelioma $n = 4$, blistering skin diseases $n = 11$ (dermatitis herpetiformis $n = 5$, pemphigus $n = 2$, pemphigoid $n = 2$, epidermolysis bullosa $n = 2$), and normal skin from various parts of the body $n = 9$.
3. Various organs with epithelial components displaying normal histology: kidney $n = 3$, liver $n = 3$, pancreas $n = 3$, parotic gland $n = 3$, prostatic gland $n = 3$, mammary gland $n = 3$, testis $n = 3$, bronchus $n = 3$, normal gastric mucosa $n = 3$, normal duodenal mucosa $n = 3$, and normal colon mucosa $n = 3$.
4. Carcinoma ductale mammae $n = 4$ and carcinoma adenomatosum coli $n = 6$.

Probes

A 518-BP fragment corresponding to positions 382–900 from the 5′ end of the human TIMP-3 cDNA (Silbiger et al. 1994) was generated by PCR from a fetal cDNA library and was designed with a T7 RNA polymerase promoter at the 3′ end and an SP6 RNA polymerase promoter at the 5′ end. Probe transcribed from TIMP-3 cDNA in sense orientation was used as a control for nonspecific hybridization. For control purposes, another TIMP-3 cDNA fragment (positions 282–917) was generated with RT-PCR using the Gene Amp RNA PCR kit (Perkin–Elmer/Roche; Branchburg, NJ). Total cellular RNA from cultured normal human skin fibroblasts was used as template (manuscript in preparation) and the fragment was subcloned to pBluescript (Stratagene; La Jolla, CA). The production and specificity of the TIMP-1 RNA probe have been described (Sudbeck et al. 1992). By FASTA alignment, highest similarities between the TIMP-3 probes and TIMP-1 and -2 were 53–55% making cross-hybridization at high stringency unlikely.

In Situ Hybridization

In vitro transcribed anti-sense and sense RNA probes were labeled with $\alpha[^{35}S]$-UTP. Sections were hybridized with probes (2.5–4 $\times$ 10^4 cpm/μl of hybridization buffer) and were washed under stringent conditions, including treatment with RNase A, as described (Saarialho-Kere et al. 1993). After autoradiography for 10–35 days, the photographic emul-

sion was developed and the slides were stained with hematoxylin and eosin. Samples of breast carcinomas were used as positive controls (Uria et al. 1994). Each sample was hybridized in at least two experiments, and a sense probe was used as a negative control. The slides were independently analyzed by two investigators.

Keratinocyte Cultures

Primary cultures of normal human epidermal keratinocytes were established from skin specimens from a woman undergoing mammoplasty for nonmalignant disease, as described previously (Boyce and Ham 1985). The cells were maintained in Keratinocyte Growth Medium (Clonetics; San Diego, CA) supplemented with epidermal growth factor (0.2 ng/ml) and bovine pituitary extract (30 μg/ml) (both from Life Technologies; Paisley, UK). Cells were incubated for 24 hr with human recombinant IL-1β (5 U/ml), TNF-α (20 ng/ml) (both from Boehringer Mannheim; Mannheim, Germany) and bovine TGF-β2 (5 ng/ml) (kindly provided by Dr. David R. Olsen, Celtrix Co., Santa Clara, CA).

HaCaT cells, transformed human epidermal keratinocytes (obtained from Dr. Norbert Fusenig, DKFZ, Heidelberg, Germany) (Boukamp et al. 1988), were cultivated in Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal calf serum. At confluence, cells were washed twice with PBS and incubated under serum-free conditions for 18–20 hr, followed by incubation with 5–50 ng/ml EGF (epidermal growth factor), 1–100 nM PMA (phorbol myristate acetate) (both from Sigma Chemical; St Louis, MO), or 0.1–10 ng/ml TGF-β1 (R & D Systems; Minneapolis, MN) for 6 hr.

RNA Analysis

Total cellular RNA was isolated from primary keratinocyte cultures using the guanidine thiocyanate–cesium chloride method (Chirgwin et al. 1979), and from HaCaT cells using the guanidine thiocyanate–phenol–chloroform extraction (Parks et al. 1988). Fifteen μg of RNA was fractionated on formaldehyde–agarose gel and transferred to nylon membranes. Northern blot hybridizations were performed as described previously (Thomas 1980) with cDNAs labeled with [α-^{32}P]-dCTP using random priming and [^{32}P]-cDNA–mRNA hybrids were visualized by autoradiography. The mRNA levels were quantitated by densitometric scanning of the X-ray films on gray scale with background subtraction using MCID software (Imaging Research; St Catharines, Ontario, Canada), and corrected for the levels of rRNA visualized by ethidium bromide staining.

Results

TIMP-3 mRNA Is Expressed in Fetal Kidney, Cartilage, Bone, and Mesenchyme

The youngest fetal sample studied was an embryo 7 weeks of age whose main organ systems had developed. Epidermis, seen as a single layer of cells, showed no signal for TIMP-3 mRNA, but expression was detected in neuroepithelium (data not shown), in developing kidney, and in the adjacent gonadal ridge (Figures 1A, 1B, and 1D), and in cells within mesenchymal tissues (data not shown). Developing bone, heart, liver, and lungs, as well as bronchial epithelium, remained negative. At 8–9 weeks of gestation, chondrocytes of hand and foot plate cartilages (Figures 2A and 2B) and vertebral bodies (data not shown) expressed TIMP-3 mRNA. In other organs the distribution of TIMP-3 mRNA remained the same. At 10 weeks, signal was again detected in chondrocytes of ribs and limbs, and surrounding mesenchymal cells were positive (data not shown). At 12 weeks of gestation, expression of TIMP-3 mRNA was seen in hypertrophic chondrocytes of developing ribs and in surrounding mesenchymal cells that become osteoblasts (Figures 2C and 2D). In the same sample, bones that were already undergoing ossification had TIMP-3-expressing osteoblasts within the newly formed bone matrix (data not shown). Unlike in mouse embryos (Apte et al. 1994a), TIMP-3 mRNA was not detected in developing epidermis or in the epithelium of gastrointestinal tract or bronchial trees (data not shown).

At 7 and 8–9 weeks of gestation, no expression of TIMP-1 mRNA was detected. However, at 12 weeks mesenchymal cells surrounding hypertrophic cartilage (Figures 2E and 2F) were positive. In addition, osteoblasts within the bone matrix showed intense signal, as described earlier (Nomura et al. 1989). Chondrocytes remained negative.

Outer Root Sheath Cells of Hair Follicles Express TIMP-3 mRNA at the Anagen Phase

Biopsies of armpit and scalp skin at 16 weeks of gestation showed hair germs and early hair buds penetrating the underlying dermis. Epidermis was devoid of signal, but epithelial cells of the hair germs showed expression of TIMP-3 mRNA (Figure 3A, Inset a). By 20 weeks, follicles of the scalp showed established morphology, with epithelial cells forming the outer root sheath and mesenchymal cells forming the dermal papilla. Cells of the outer root sheath were consistently positive for TIMP-3 mRNA (Figure 3B, Inset b). In trunk skin, signal was again detected in hair germs and buds, and some follicles already in a more advanced stage of development showed signal in the outer root sheath cells (data not shown). In skin biopsies at 21 and 23 weeks of gestation, outer root sheath cells of each follicle were positive for TIMP-3 mRNA in the biopsies of both scalp and trunk (data not shown).

In adult hair follicles, TIMP-3 gene was activated during the early anagen (growing) phase and the expression persisted until the follicle entered the catagen phase and started to regress. TIMP-3 mRNA localized mainly to basal cell layer of the outer root sheath in the lower portion of the follicle (Figure 3C, Inset c). In some anagen follicles, a few pale-staining medulla

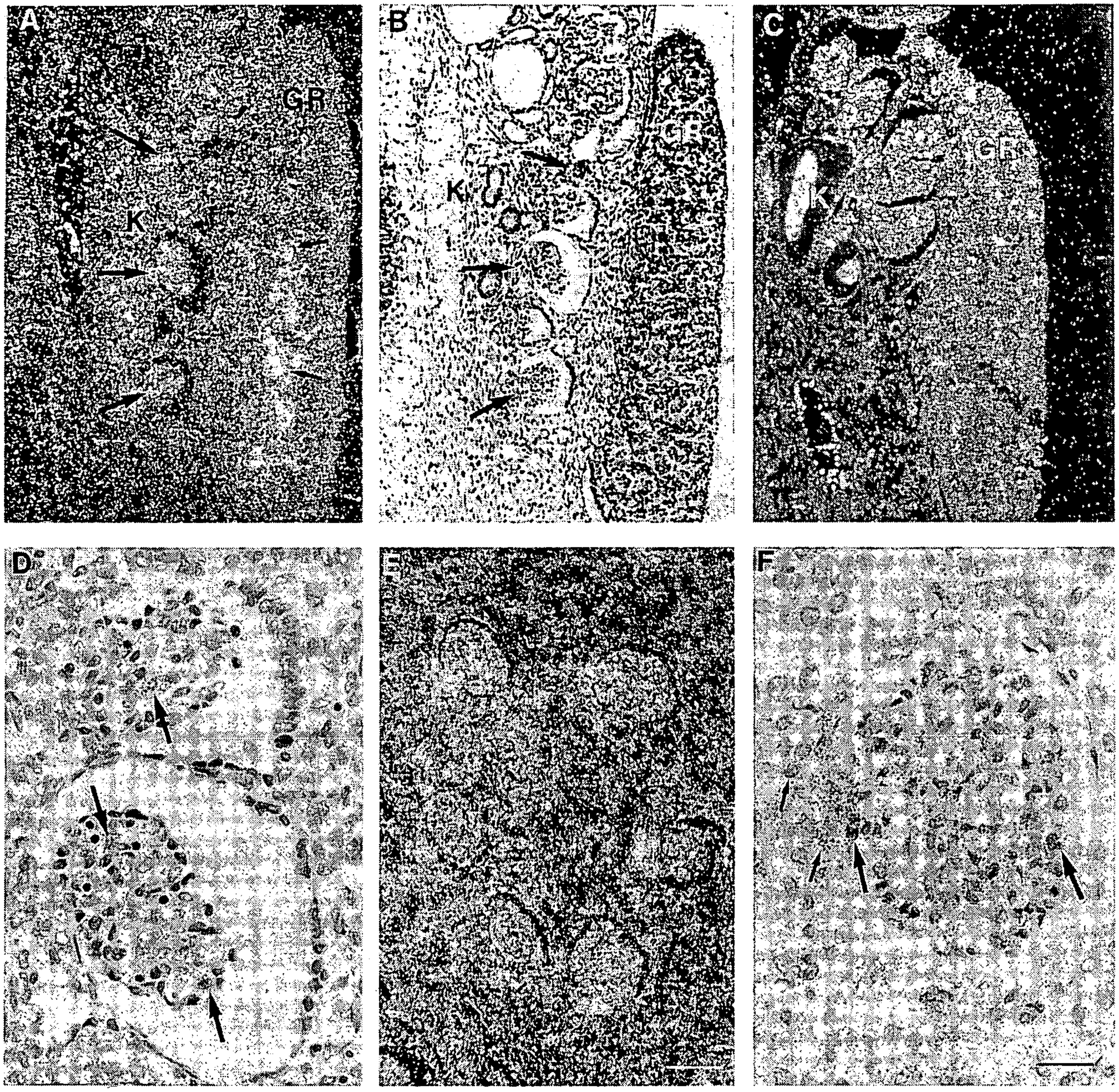

Figure 1 Expression of TIMP-3 mRNA in fetal and adult kidney. Samples were hybridized with TIMP-3 cRNA antisense (**A,B,D–F**) or TIMP-3 sense (**C**) probe as described in Materials and Methods. (**A**) Darkfield image of embryonal kidney (K) and gonadal ridge (GD) at 7 weeks of gestation. TIMP-3 mRNA is detected in cells of developing kidney (arrows) and gonadal ridge (small arrows). (**B**) Corresponding brightfield image. (**C**) A sense control. (**D**) High-power image of TIMP-3 mRNA in cells of developing kidney (arrows). In adult kidney, cortex expression of TIMP-3 mRNA is detected in both glomeruli and tubules, as seen in darkfield (**E**) and high power brightfield (**F**) images. Glomerular cells (arrows) and tubule epithelial cells (small arrows) express TIMP-3 mRNA. Bars: **A–E** = 34 μm; **D,F** = 8 μm.

cells within the hair matrix were also positive (Figure 3C). No expression was seen in telogen (resting) follicles (data not shown).

TIMP-3 was not upregulated during re-epithelialization of blistering skin diseases, and expression was not detected in normal epidermis or in sebaceous and sweat glands. However, expression was often seen in fibroblast-like stromal cells surrounding sweat glands and some blood vessels (data not shown). TIMP-1 mRNA was commonly detected in sebaceous glands and in perivascular cells (data not shown) but only occasionally in some outer root sheath cells of anagen hair follicles (Figure 3D). Expression was not detected in fetal hair follicles.

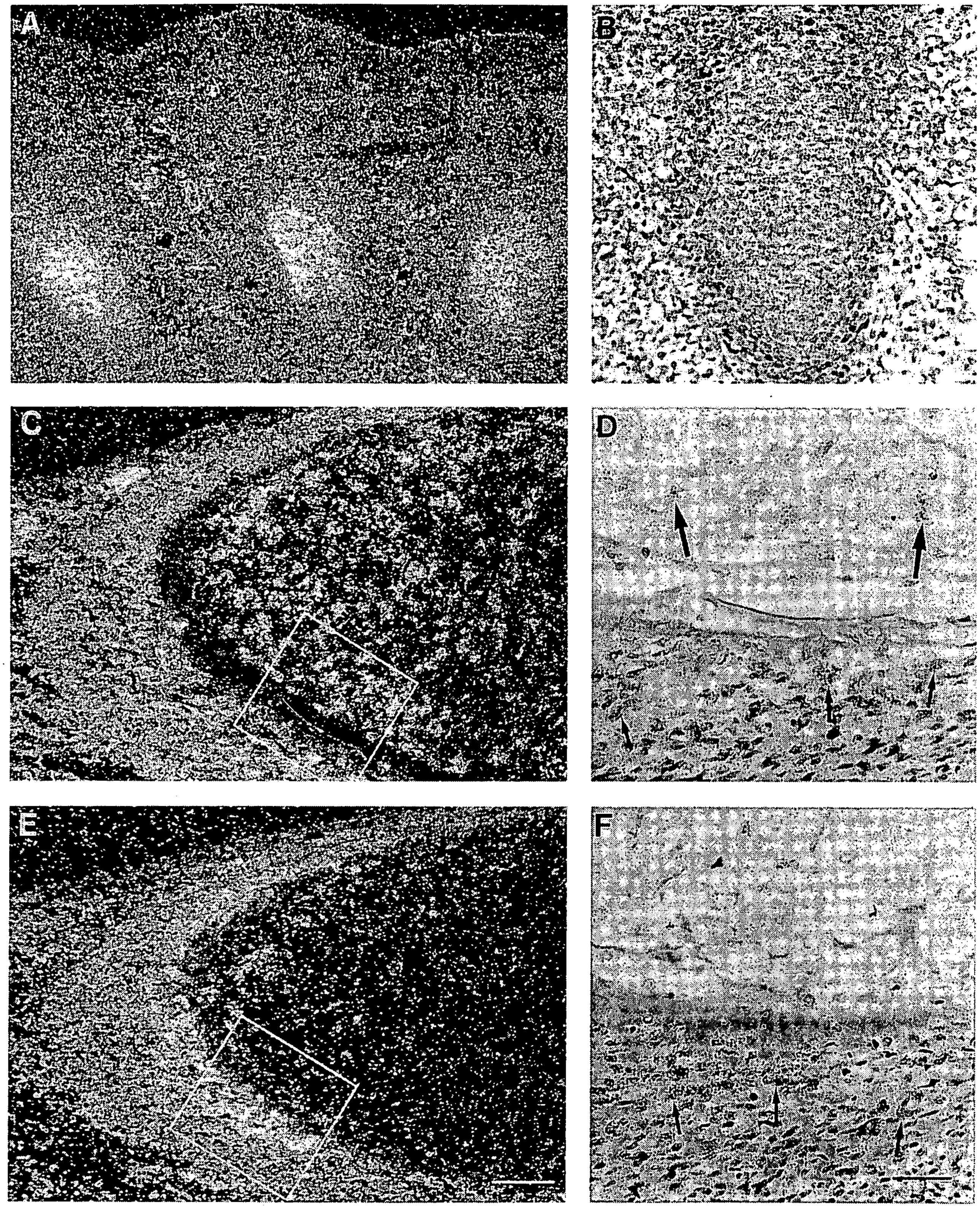

Figure 2 Fetal hypertrophic chondrocytes express TIMP-3, but not TIMP-1 mRNA. Samples were hybridized with TIMP-3 (**A–D**) and TIMP-1 (**E,F**) anti-sense probes. (**A,B**) A sample of a fetus at 8–9 weeks of gestation with TIMP-3-expressing chondrocytes of foot plates. (**C,D**) Expression of TIMP-3 mRNA in a developing rib at 12 weeks. Both hypertrophic chondrocytes (arrows) and mesenchymal cells (small arrows) that became osteoblasts express TIMP-3 mRNA. (**E,F**) TIMP-1 expression is limited to the mesenchymal cells (small arrows). **A**, **C**, and **E** are dark-field images. Bars: **A,C,E** = 34 μm; **B,D,F** = 17 μm.

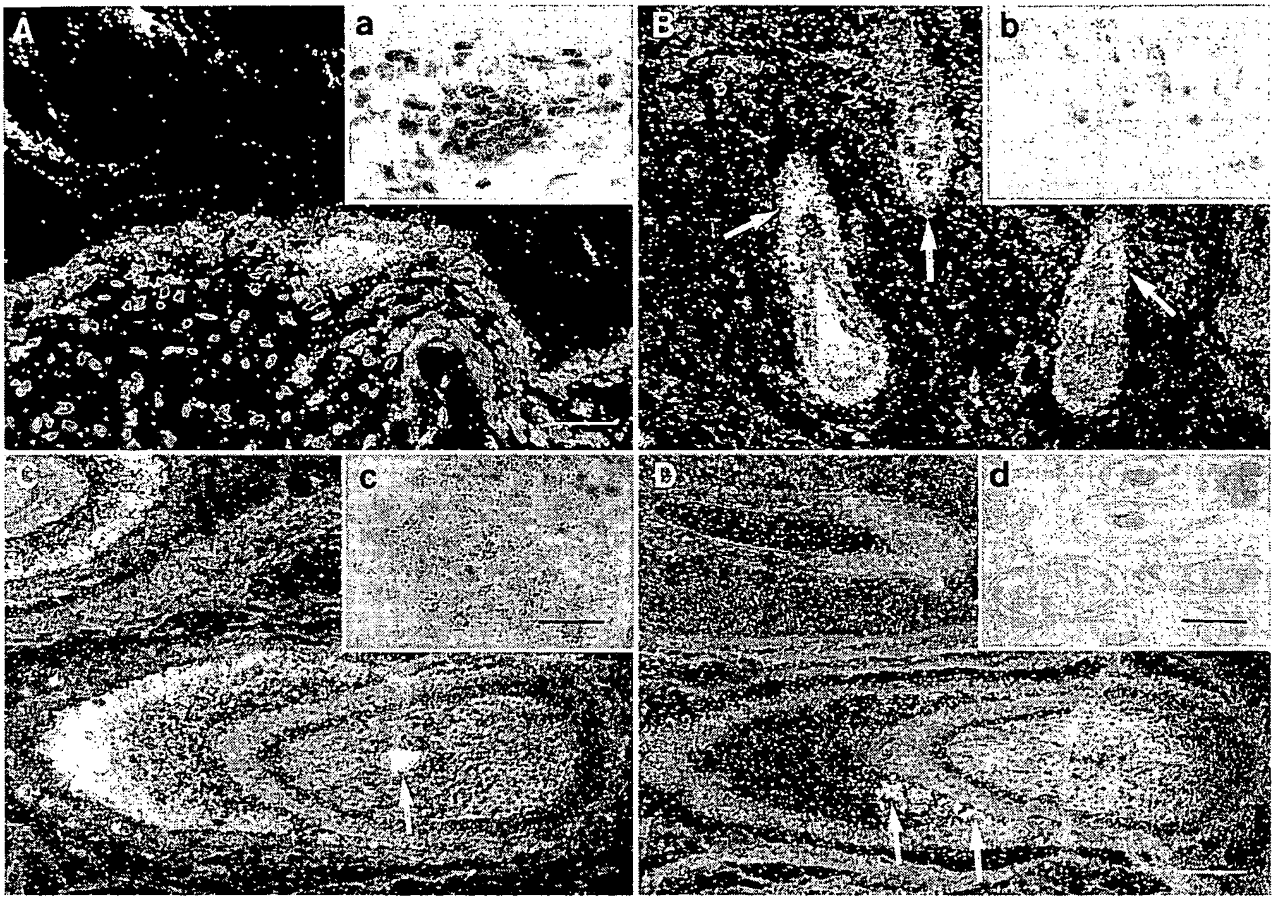

Figure 3 TIMP-3 is expressed during the hair growth cycle. In situ hybridizations with TIMP-3 (**A–C, Inset d**) and TIMP-1 anti-sense probe (**D**) were performed as described in Materials and Methods. (**A**) Skin of a fetus at 16 weeks of gestation shows expression of TIMP-3 mRNA in the epithelial cells of a hair germ (**Inset a**). (**B**) At 20 weeks of gestation, fetal scalp has many structurally complete hair follicles. Expression of TIMP-3 is detected in the outer root sheath cells of epidermal origin (arrows). Lower magnification shows a brightfield image of fetal scalp (**Inset b**). (**C, Inset c**) Outer root sheath cells of adult anagen hair follicles express TIMP-3 mRNA consistently. A few pale-staining cells in the middle of the hair matrix are also positive for TIMP-3 (arrows). (**D**) TIMP-1 mRNA is occasionally detected in outer root sheath cells (arrows) of anagen follicles. (**Inset d**) Lower magnification of adult scalp. **A–D** are darkfield images. Bars: **A** = 17 μm; **B–D** = 34 μm; **a,c** = 8 μm; **b,d** = 170 μm.

TIMP-3 Expression Is Induced by TGF-β in Primary Human Keratinocytes

Because TIMP-3 was expressed in hair follicles, we studied its expression in keratinocytes treated with various growth factors known to influence hair growth cycle. Primary human epidermal keratinocytes were treated with TGF-β2, IL-1β, and TNF-α, and levels of TIMP-3 mRNAs were assayed by Northern blot hybridizations. As shown in Figure 4, epidermal keratinocytes expressed clearly detectable levels of three distinct TIMP-3 mRNAs (2.4, 2.8, and 4.8 KB), and the TIMP-1 probe detected a single 0.9-KB mRNA. Interestingly, treatment of epidermal keratinocytes with TGF-β2 (5 ng/ml) markedly (4.3-fold) enhanced TIMP-3 mRNA abundance in these cells. In contrast, IL-1β (5 U/ml) and TNF-α (20 ng/ml) had no marked effect (Figure 4). It has previously been shown that epidermal keratinocytes in culture express TIMP-1 (Petersen et al. 1992). However, none of the treatments markedly altered the levels of TIMP-1 mRNA (Figure 4). HaCaT cells, transformed human epidermal keratinocytes, expressed basally low levels of TIMP-3 mRNA. Treatment with EGF, PMA, or TGF-β1 did not alter the levels of TIMP-3 mRNA (data not shown).

TIMP-3 Is Expressed in Cancer Tissues

To determine whether TIMP-3 also plays a role in the behavior of benign and malignant skin tumors, samples of hair follicle-derived tumors, trichofolliculomas and trichoepitheliomas, and epidermal skin cancers were examined. Interestingly, no signal for TIMP-3 mRNA was detected in the benign tumors (data not shown). Basal cell carcinomas with keratotic (hair-like) differentiation were also negative, whereas in

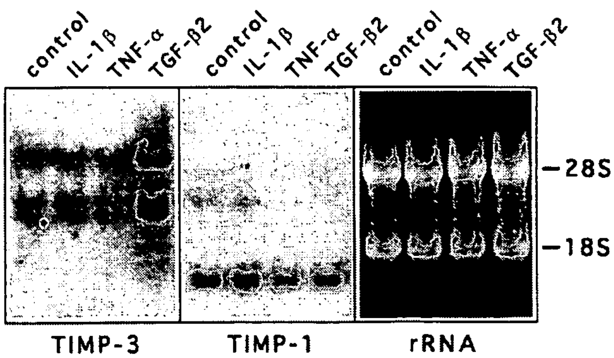

Figure 4 Expression of TIMP-3 mRNAs in epidermal keratinocytes is enhanced by TGF-β. Human primary epidermal keratinocytes were maintained as described in Materials and Methods and treated for 24 h with IL-1β (5 U/ml), TNF-α (20 ng/ml), and TGF-β2 (5 ng/ml). TIMP-1 and -3 mRNA levels were examined by Northern blot hybridizations of 15 μg of total RNA, and 18S and 28S rRNAs were visualized by ethidium bromide staining. IL-1β and TNF-α had no marked effect on TIMP-3 mRNA expression, whereas TGF-β2 induced the expression by 4.3-fold. None of these cytokines markedly altered TIMP-1 mRNA levels.

four of five infiltrative basal cell carcinomas TIMP-3 mRNA was detected in tumor cells at the margins of this aggressively growing tumor. In these samples, TIMP-3 mRNA was also detected in areas showing nodular tumor growth (Figure 5A, Inset a) but not in stromal cells. In squamous cell carcinomas, all of which were well- or rather well-differentiated, some stromal cells located diffusively adjacent to the tumor expressed TIMP-3 mRNA (Figures 5C and 5D, Inset c), while malignant cells were negative. There was no correlation between the number of cells expressing TIMP-3 mRNA and the histopathology of the tumor. As in the samples representing normal skin, TIMP-3 mRNA was present in fibroblast-like cells surrounding sweat glands deeper in the dermis.

Normal gastrointestinal mucosa and mammary gland showed no signal for TIMP-3 mRNA. However, in samples of colon carcinoma intense expression was detected in both macrophages and spindle-like fibroblasts adjacent to the tumor tissue (data not shown). In agreement with the results of Byrne et al. (1995), myoepithelial cells as well as some fibroblasts surrounding tumor nodules of intraductal mammary carcinoma consistently expressed TIMP-3, whereas tumor cells remained negative (Figures 5E and 5F). In both colon and mammary carcinomas expression of TIMP-1 co-localized with that of TIMP-3 (data not shown).

Constitutive expression of TIMP-3 mRNA was also studied in some other organs with epithelial structures. In normal adult kidney, tubule epithelial and glomerular cells expressed TIMP-3 mRNA (Figures 1E and 1F). However, the glandular epithelia of liver, pancreas, parotid gland, testis, and prostate were negative. In addition, bronchial epithelium and adult bronchial cartilage were devoid of signal. The abundance of mRNA in Northern blot hybridizations of these organs (Apte et al. 1994b; Wick et al. 1994; Wilde et al. 1994) can be explained by the presence of various amounts of TIMP-3-expressing stromal cells, especially if any inflammation is present.

Discussion

The controlled physiological degradation of the ECM requires a fine balance between MMPs and their inhibitors, whereas in processes such as arthritis and tumor invasion MMP activity predominates, leading to excessive tissue degradation. There are accumulating data on the role of TIMPs and synthetic MMP inhibitors in suppressing tumor growth and invasion. Additional functions independent of metalloproteinase inhibitory activity have also been reported: TIMP-1 and -2 are anti-angiogenic (Moses et al. 1990; Johnson et al. 1994) and they possess growth-promoting activity towards a number of cell types (Hayakawa et al. 1992,1994) . The role of TIMP-3 in development and connective tissue turnover has thus far been studied mostly in cell cultures, in animal models, and by analyzing mRNA from tissues by Northern hybridization. In the present study we have extended the analysis of TIMP-3 in vivo by examining its expression in human tissues. We also show that the levels of TIMP-3 transcripts are induced in human primary keratinocytes by TGF-β.

Various metalloproteinases and their inhibitors are involved in mammalian development. During the murine peri-implantation period, interstitial collagenase and stromelysin-1 mRNAs are produced by the embryo (Brenner et al. 1989). In later stages of murine embryogenesis, collagenase expression is restricted to hypertrophied chondrocytes, osteoblasts, endothelial cells, and osteoclasts of developing bones (Mattot et al. 1995). Rodent collagenase is suggested to be analogous to human collagenase-3, and these findings are consistent with our recent report on the expression of human collagenase-3 in hypertrophic chondrocytes and osteoblasts during human fetal bone development (Johansson et al. 1997). The 72-kD gelatinase is expressed widely in murine mesenchymal tissues, whereas 92-kD gelatinase mRNA production is limited to osteoclastic cells (Reponen et al. 1994). TIMP-1 and -2 are also predominantly expressed in osteogenic tissues, with some expression of TIMP-1 mRNA also in kidney, lung, ovary, and amnion (Nomura et al. 1989; Flenniken and Williams 1990; Mattot et al. 1995). TIMP-3 transcripts were found at sites of active matrix remodeling, such as developing bone and hair follicles. Co-localization of MMPs and their inhibitors in these areas suggests a coordinate process of ECM for-

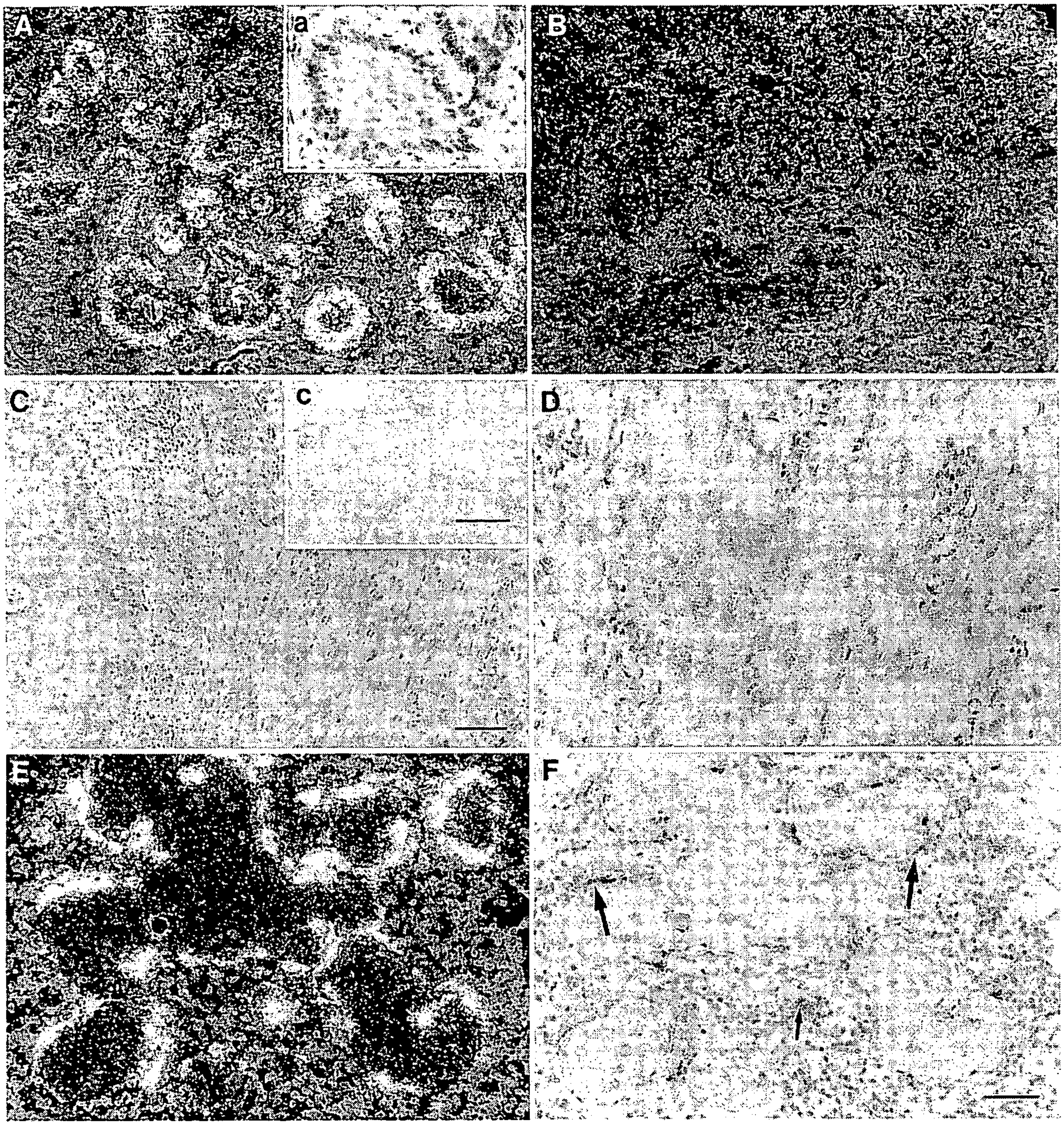

Figure 5 Expression of TIMP-3 mRNA in malignant tumor tissues. Samples were hybridized with TIMP-3 anti-sense and sense probes as described. **(A,a)** A basal cell carcinoma. Tumor cells at the margins of tumor nodules express TIMP-3 mRNA. No expression is detected in stromal cells. **(B)** Serial section hybridized with a sense probe. **(C)** Edge of a well-differentiated squamous cell carcinoma of the skin. **(c)** Lower magnification of the tumor. **(D)** TIMP-3 mRNA is not expressed by tumor cells but by fibroblastic stromal cells adjacent to the tumor. **(E,F)** Intraductal mammary carcinoma. TIMP-3 mRNA is expressed by myoepithelial cells (arrows) surrounding tumor cells and by some adjacent fibroblasts (small arrow). **A**, **B**, and **E** are darkfield images. Bars: **A–C** = 34 μm; **a,D–F** = 17 μm; **c** = 170 μm.

mation and degradation in the development and maintenance of normal tissue architecture. TIMP-3 does not appear to have a major role in the epithelial folding and branching during human fetal development, in contrast to the results of Apte et al. (Apte et al. 1994a) in mouse embryos. However, their samples represented murine embryos of 12.5 to 14.5 days of gestation as well as newborn mice, and we cannot exclude

the possibility that in human development TIMP-3 is very transiently expressed during a time period that is not covered by our samples.

Expression of TIMP-3 was detected throughout fetal hair development, starting from the hair germ stage. Hair germ formation begins in the scalp and face during the third month of gestation and gradually extends in a cephalocaudal direction. The germ consists of a group of epidermal basal cells that protrude into the dermis, forming a hair bud. Mesenchymal cells beneath each bud give rise to the dermal papilla. Further differentiation leads to the formation of the hair cuticle with the surrounding layers of inner and outer root sheath. From the beginning of the fifth month of gestation, different developmental stages are found, ranging from mature follicles to new developing ones (Lever and Schaumburg–Lever 1990). The factors that regulate the process of follicle development and growth cycle are not well understood, but they include epithelial–mesenchymal interactions and cytokines, such as epidermal growth factor (EGF), transforming growth factor-α (TGF-α), and members of the TGF-β family (Messenger 1993). The expression of TIMP-3 is stimulated in mouse cells by various agents, including PMA, EGF, TGF-β, dexamethasone, and TNF-α (Leco et al. 1994; Sun et al. 1995). However, in human primary keratinocytes only TGF-β induced expression of TIMP-3, while IL-1β and TNF-α had no effect. None of these cytokines markedly affected TIMP-1 expression. TGF-β2 mRNA co-localizes with TIMP-3 in the basal cells of the outer root sheath (Schmid et al. 1996), and since TGF-β inhibits growth of cultured hair follicles (Philpott et al. 1990) it may induce TIMP-3 to control follicle growth and degradation of the surrounding ECM.

Immunoreactivity for interstitial collagenase and matrilysin (MMP-7) has been detected in human hair follicles (Karelina et al. 1994; McGowan et al. 1994). Cultured hair follicles synthesize and secrete various MMPs, including interstitial collagenase, stromelysin-1, and gelatinases (Weinberg et al. 1990; Goodman and Ledbetter 1992; Paus et al. 1994). Cyclic expression of TIMP-1 in the inner root sheath of mouse hair follicles has been reported, with gene activation during mid-anagen phase (Kawabe et al. 1991). Our results demonstrate constitutive expression of TIMP-3 in both fetal and adult anagen follicles. TIMP-3 appears to contribute to the inhibition of proteolysis associated with degradation of the dermal matrix during the initial hair follicle formation, and later during the early anagen phase as the cells proliferate and invade the deeper dermis. On the basis of our studies, TIMP-1 does not have a consistent role in the growth cycle of human hair follicle. Our findings on the expression patterns of TIMP-1 and -3 in human tissues indicate that there are differences among species, and therefore the results obtained using animal models can not be directly applied to humans.

In cutaneous squamous cell carcinomas as well as mammary and intestinal carcinomas, TIMP-3 mRNA was detected in stromal cells adjacent to the malignant tumor, which is a common expression pattern for both MMPs and TIMPs. TIMP-3 was not expressed in the benign tumors and the nonaggressive keratotic basal cell carcinomas, but the signal was distinct in the infiltrative subtype and was localized to the malignant cells at the margins of tumor islands. In contrast, both TIMP-1 and -2 are detected only in the stromal cells of surrounding basal cell carcinoma (Childers et al. 1987; Wagner et al. 1996). Furthermore, expression of TIMP-2 mRNA is lower in cutaneous squamous cell carcinomas and infiltrative subtypes of basal cell carcinoma, compared to less infiltrative subtypes (Poulsom et al. 1993; Wagner et al. 1996). In cutaneous malignant melanomas, induction of both TIMP-1 and -3 mRNA expression in vivo correlates with increased depth of invasion (manuscript in preparation). Therefore, malignant transformation appears to induce the TIMP-3 gene, and in skin tumors invasive growth is associated with enhanced TIMP-3 expression, concomitantly with increased expression of matrix metalloproteinases (Ray and Stetler–Stevenson 1994). This suggests a role for TIMP-3 in the inhibition of metalloproteinase-mediated basement membrane and matrix degradation required for malignant growth.

In this study, TIMP-3 and -1 were differentially expressed during human fetal development. Furthermore, they were differently regulated in keratinocyte cultures by various growth factors. Further studies are needed to determine the level and specific functions of TIMP-3 protein in various human tissues. On the basis of the expression pattern of TIMP-3 mRNA, TIMP-3 appears to protect the matrix from proteolytic activity and thus regulate normal tissue turnover and inhibit malignant growth. Our results demonstrate a role for TIMP-3 in human fetal development and in remodeling processes of the extracellular matrix.

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The New Human Tissue Kallikrein Gene Family: Structure, Function, and Association to Disease*

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ABSTRACT

The human tissue kallikrein gene family was, until recently, thought to consist of only three genes. Two of these human kallikreins, prostate-specific antigen and human glandular kallikrein 2, are currently used as valuable biomarkers of prostatic carcinoma. More recently, new kallikrein-like genes have been discovered. It is now clear that the human tissue kallikrein gene family contains at least 15 genes. All genes share important similarities, including mapping at the same chromosomal locus (19q13.4), significant homology at both the nucleotide and protein level, and similar genomic organization. All genes encode for putative serine proteases and most of them are regulated by steroid hormones. Recent data suggest that at least a few of these kallikrein genes are connected to malignancy. In this review, we summarize the recently accumulated knowledge on the human tissue kallikrein gene family, including gene and protein structure, predicted enzymatic activities, tissue expression, hormonal regulation, and alternative splicing. We further describe the reported associations of the human kallikreins with various human diseases and identify future avenues for research. (*Endocrine Reviews* **22:** 184–204, 2001)

I. Introduction

KALLIKREINS are a group of serine proteases that are found in diverse tissues and biological fluids. The term "Kallikrein" was introduced in the 1930s by Werle and colleagues (1, 2) who found high levels of their original isolates in the pancreas (in Greek, the "Kallikreas"). The kallikrein enzymes are now divided into two major categories: plasma kallikrein and tissue kallikrein (3, 4). These two categories differ significantly in their molecular weight, substrate specificity, immunological characteristics, gene structure, and type of kinin released. Plasma kallikrein or Fletcher factor (official symbol KLKB1)[1] is encoded by a single gene, which is located on human chromosome 4q35 (5, 6). The gene is composed of 15 exons and encodes for an enzyme that releases the bioactive peptide bradykinin from a high molecular weight precursor molecule (high mol wt kininogen) produced by the liver. Plasma kallikrein is exclusively expressed by liver cells. The function of plasma kallikrein includes its participation in the process of blood clotting and fibrinolysis and, through the release of bradykinin, in the regulation of vascular tone and inflammatory reactions (7). Plasma kallikrein will not be discussed further in this review since the gene encoding for this enzyme has no similarities with the tissue kallikrein genes and clearly, is not a member of this multigene family. A historical perspective on the discovery of the kallikrein-kinin system and bradykinin has recently been published (8).

Tissue kallikreins are members of a large multigene family and demonstrate considerable similarities at the gene and protein level as well as in tertiary structure. In this review, we will describe recent developments, exclusively pertinent to the human family of enzymes.

The term "kallikrein" is usually used to describe an enzyme that acts upon a precursor molecule (kininogen) for release of a bioactive peptide (kinin) (7–10). Another term that is also frequently used to describe these enzymes is

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[1] KLK, kallikrein; KLK-L, kallikrein-like; EMSP1, enamel matrix serine proteinase 1; hGK-1, human glandular kallikrein-1; HSCTE, human stratum corneum tryptic enzyme; HSCCE, human stratum corneum chymotryptic enzyme; TADG-14, tumor-associated differentially expressed gene-14; TLSP, trypsin-like serine protease; NES1, normal epithelial cell-specific 1 gene; PRSS, protease serine; PRSSL, protease serine-like; HRE, hormone response element; ARE, androgen response element; CNS, central nervous system; HUGO, human genome organization; uPA, urokinase type plasminogen activator; TGF-β, transforming growth factor β; PSA, prostate specific antigen.

"kininogenases." The term "kininase" is used to describe other enzymes that can inactivate kinins. Among the known human and animal tissue kallikreins, only one enzyme has the ability to release efficiently a bioactive kinin from a kininogen. In humans, this enzyme is known as pancreatic/renal kallikrein or, with the new nomenclature, as the KLK1 gene, encoding for human kallikrein 1 (hK1 protein) (9–12). This enzyme acts upon a liver-derived kininogen (low mol wt kininogen) to release lysyl-bradykinin (also known as kallidin), which is involved in the control of blood pressure, electrolyte balance, inflammation, and other diverse physiological processes. Tissue kallikrein (hK1) may further enzymatically digest other substrates, including growth factors, hormones, and cytokines, to mediate pleiotropic effects (7).

It should be emphasized that the generic term "tissue kallikrein" *is not* restricted to the description of enzymes that release bioactive peptides from precursor molecules. The term is used to describe a group of enzymes with highly conserved gene and protein structure, which also share considerable sequence homology and colocalize in the same chromosomal locus as the KLK1 gene. In this review, the term "kallikrein" will be used to describe a family of 15 genes that have a number of striking similarities, as outlined in point format in Table 1 (13). The use of the term "kallikrein" *does not* necessarily imply that any of these family members (with the exception of KLK1) have kininogenase activity. In fact, for human family members that have been functionally tested, it was found that they possess very low (hK2) (14, 15) or no kininogenase activity [prostate-specific antigen (PSA)] (14). These enzymes are grouped together with KLK1, based on the similarities outlined in Table 1.

II. The Human and Rodent Families of Kallikrein Genes

The tissue kallikrein literature can be roughly separated into various periods as follows. Early in the 1920s and 30s, researchers discovered the basic components of the kallikrein-kinin system and identified the molecular structure of bradykinin and kallidin (lysyl-bradykinin) in the 1960s (8). The molecular biology of the tissue kallikrein gene family was worked out in detail in both the human and rodents in the 1980s (16–19). It was then concluded that the mouse and rat gene families were composed of many genes, clustered in the same chromosomal locus. In particular, the mouse tissue kallikrein gene family is localized on chromosome 7 and consists of 24 genes, of which at least 14 encode for active proteins (the remaining being pseudogenes) (16, 20–22). The area on chromosome 7 encompassing the mouse kallikreins is homologous to an area on human chromosome 19q13.4 that harbors the human kallikrein gene family. The rat tissue kallikrein gene family is composed of approximately 20 homologous genes of which at least 10 are expressed (18, 23–30).

Most of the rodent tissue kallikreins are expressed in the salivary glands, but a few, including the prostate, pituitary gland, and endometrium, have more diverse tissue expression (7, 9, 31–33). It is not the purpose of this review to describe in detail the rodent or other animal tissue kallikrein gene families. Excellent reviews on this subject already exist (9, 16, 17, 21, 22).

The human tissue kallikrein gene family was also discovered in the 1980s and it was then concluded that the entire family is composed of only three genes, namely KLK1, encoding for pancreatic/renal kallikrein (hK1 protein), the KLK2 gene, encoding for human glandular kallikrein 2 (hK2), and the KLK3 gene, encoding for PSA (hK3) (34–38). The major interest in human kallikreins lies in the very restricted tissue expression of hK2 and hK3 in the prostate, which qualifies them as candidate biomarkers for prostatic diseases (39–43). hK3 (PSA), in particular, has gained prominence in recent years as the most valuable tumor marker ever discovered and is currently used widely for the diagnosis, monitoring, and population screening for prostate cancer (44–51). The introduction of this test has had a major impact on prostate cancer diagnosis and monitoring and this field is still evolving (52, 53). More recently, PSA applications have extended beyond the prostate, including breast and other cancers (54–57). Over the last few years, human glandular kallikrein 2 is emerging as an additional prostatic and breast cancer biomarker, and it is now clear that it can supplement PSA testing for improved identification and differential diagnosis of prostate cancer (43, 58–66). It is thus logical to exploit the possible applications of other members of this gene family for cancer and other disease diagnosis and monitoring.

In the last 3 yr, we have witnessed the emergence of new knowledge related to the human kallikrein gene family (13). Independent researchers have cloned a number of new serine protease genes that show significant homologies with the classical human kallikreins; in addition, when these new protease genes were mapped, they were found to colocalize in the known human kallikrein gene locus on chromosome 19q13.3-q13.4 (67–90). The recent detailed molecular description of the human kallikrein gene locus (67, 68) enabled us to construct a physical map containing 15 genes that share

TABLE 1. Similarities between members of the new human kallikrein gene family

1. All genes localize to the same chromosomal region (19q13.4).
2. All genes encode for putative serine proteases with a conserved catalytic triad (histidine, aspartic acid, and serine in the appropriate positions).
3. All genes have five coding exons (some members contain one or more 5'-untranslated exons).
4. Coding exon sizes are similar or identical.
5. Intron phases are fully conserved among all 15 human members and among members of the rodent kallikrein gene families.[a]
6. All genes have significant sequence homologies at the DNA and amino acid levels (40–80%).
7. Many of these genes are regulated by steroid hormones.

[a] Intron phase refers to the location of the intron within the codon: intron phase I, the intron occurs after the first nucleotide of the codon; II, the intron occurs after the second nucleotide; 0, the intron occurs between codons.

significant structural similarities (Table 1). Some of these genes appear to be related to breast, ovarian, and other human cancers, and a few of them appear to encode for functional tumor suppressor genes. In view of these very recent developments, we will describe, in this review, the knowledge that has accumulated on these genes, with special emphasis on the structure of the genes and proteins, their tissue expression and hormonal regulation, and their connection to various human diseases. Where possible, functional aspects of these enzymes will also be described. We hope that the summary of these new findings on the human kallikrein gene family will facilitate further research toward better understanding their physiological function, their pathophysiology and connection to human diseases, and their possible applications in the diagnosis and monitoring of various malignancies and their future suitability as therapeutic targets.

III. Nomenclature

Until 2–3 yr ago, only three human kallikrein genes were recognized: the pancreatic/renal kallikrein (KLK1), the human glandular kallikrein 2 (KLK2), and PSA (KLK3). Rittenhouse and co-workers (43, 49) have recently published the revised nomenclature for these three genes. New developments led to the identification of 15 different genes exhibiting significant homologies and other similarities, as described in Table 1 (13). Since many of these genes were cloned independently by different investigators, various empirical names were initially used for their description.

The Human Genome Organization (HUGO) has recently proposed guidelines for human gene nomenclature. Initially, some members of the new kallikrein gene family were classified by HUGO along with other serine proteases under the prefix "PRSS", standing for "protease serine." It is now clear that this designation does not serve well the needs of the future since members of this multigene family are classified together with other serine proteases that map in different locations of the genome.

The construction of the first detailed map of the human kallikrein gene locus (13, 67, 68) allows for a more rational assignment of official gene symbols. Since the rodent and other animal species kallikrein multigene families were known before 1992, an international working party had reached agreement in 1992 on uniform nomenclature of the animal kallikreins and the three human kallikreins known at that time (91). Based on this paradigm and the guidelines of HUGO (for details please visit the Website: http://www.gene.ucl.ac.uk/nomenclature/), an international group of scientists working in the field agreed to adopt a nomenclature for the newer human kallikreins, consistent with that already defined for KLK1–3, as shown in Table 2 (92). In the same table, we also include previous symbols based on the PRSS system as well as names originally proposed by the discoverers of these genes (93–100). Gene numbering starts from centromere to telomere on chromosome 19q13.4 with the exception of the three classical kallikreins for which the existing nomenclature was retained and one newly discovered gene, which maps between KLK1 and KLK2 genes (69). It is possible that, in the future, new members of this gene family may be identified, either centromeric to KLK1 or telomeric to KLK14 (see below). If new kallikrein genes are identified in this locus, they will be sequentially numbered, starting with KLK16.

IV. The Human Kallikrein Gene Locus

A. Locus organization

The availability of linear genomic sequences around chromosome 19q13.3–q13.4 from the human genome project (the sequences were generated by the Lawrence Livermore National Laboratory) allowed the precise localization of the 15 members of the new human kallikrein gene family with high accuracy (±1 nucleotide) (68) (Fig. 1). The three classical kallikreins, KLK1, KLK3, and KLK2, cluster together within a 60-kb region, as previously described by Riegman *et al.* (36,

TABLE 2. Proposed new nomenclature for human kallikreins

New gene symbol[a,b]	Previous gene symbol(s)	New protein symbol	Other protein names/symbols	GenBank accession no.	Reference
KLK1	KLK1	hK1	Pancreatic/renal kallikrein, hPRK	M25629, M33105	34, 93
KLK2	KLK2	hK2	Human glandular kallikrein 1, hGK-1	M18157	94
KLK3	KLK3	hK3	Prostate-specific antigen, PSA	X14810, M24543, M27274	95–97
KLK4	PRSS17, KLK-L1, KLK4	hK4	Prostase, KLK-L1 protein, EMSP1	AF113141, AF135023, AF148532	70–72, 79
KLK5	KLK-L2	hK5	KLK-L2 protein; HSCTE	AF135028, AF168768	80, 81
KLK6	PRSS9	hK6	Zyme, protease M, neurosin	AF013988, AF149289, U62801, D78203	73, 74, 82, 83
KLK7	PRSS6	hK7	HSCCE	L33404, AF166330	84, 85
KLK8	PRSS19	hK8	Neuropsin; ovasin; TADG-14	AB009849, AF095743, AB010780, AF055982	86, 98
KLK9	KLK-L3	hK9	KLK-L3 protein	AF135026	67
KLK10	PRSSL1, NES1	hK10	NES1 protein	AF055481, NM_002776	76, 99, 87
KLK11	PRSS20	hK11	TLSP/hippostasin	AB012917, AF164623	88, 89, 100
KLK12	KLK-L5	hK12	KLK-L5 protein	AF135025	77
KLK13	KLK-L4	hK13	KLK-L4 protein	AF135024	78
KLK14	KLK-L6	hK14	KLK-L6 protein	AF161221	90
KLK15		hK15		AF242195	69

[a] The order of the genes on chromosome 19q13.4 is shown in Fig. 1.
[b] For full gene names, see abbreviation footnote.

37). and Richards *et al.* (35). Another newly discovered gene, KLK15, maps between KLK1 and KLK2 (69). The remaining kallikrein genes are aligned within this locus, as shown in Fig. 1, without intervention by other genes. The direction of transcription is from telomere to centromere with the exception of KLK3 and KLK2. The genomic lengths of all these genes are relatively small, ranging from 4–10 kb. It is unlikely that this locus harbors more kallikrein-like genes either centromeric from KLK1 or telomeric from KLK14. The next neighboring gene to KLK1 is testicular acid phosphatase (ACPT; GenBank Accession no. AF321918), which is not related to kallikreins. The next neighboring gene from KLK14 is Sigelec 9 (101). Siglecs belong to the immunoglobulin superfamily and encode for transmembrane receptors that have the ability to bind sialic acid (102, 103). These genes have no structural or functional relationship to the human kallikreins.

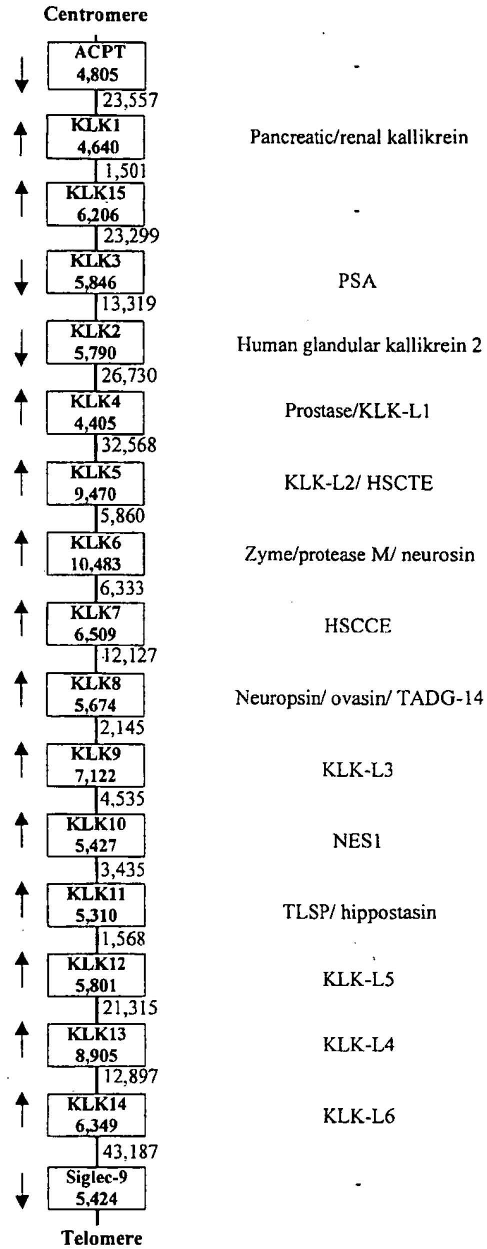
B. Gene organization

All members of the new human kallikrein multigene family encode for serine proteases. All genes consist of five coding exons, as shown in Fig. 2. The organization of all genes is very similar, with the first coding exon having a short 5′-untranslated region, the second exon harboring the amino acid histidine of the catalytic triad toward the end of the exon, the third exon harboring the aspartic acid of the catalytic triad around the middle, and the fifth exon harboring the serine of the catalytic triad, at the beginning of the exon. Beyond the stop codon, there is a 3′-untranslated region of variable length.

While it is certain that the classical kallikreins do not have 5′-untranslated exons, most other members of this multigene family have one or two 5′-untranslated exons, as shown in Fig. 2. It is possible that some other members of this gene family also harbor 5′-untranslated exons, which have not as yet been identified. In addition, the 3′-untranslated region of many of these genes is sometimes variable, giving rise to variants with different mRNA lengths, but encoding for the same protein (variant kallikrein transcripts are described under a separate heading). It is thus possible that the actual lengths of these genes, as shown in Figs. 1 and 2, may change slightly in the future.

Although the intron lengths of these genes vary considerably, the exon lengths are quite comparable or identical. Additionally, the intron phases between coding exons of all these genes (and those of the rodent kallikreins) are completely conserved among all members, with phases I–II–I–O. The intron phases are defined in Fig. 2.

Although TATA boxes have been identified within the proximal promoter of the classical kallikrein genes (Table 3), no such elements were found for most of the other kallikreins. This may be due to the absence of these elements or to the fact that the proximal promoter of some of these genes has not been accurately defined due to the presence of as yet unidentified 5′-untranslated exons. This issue merits further investigation. Classical (AATAAA) or variant polyadenylation signals have been identified 10–20 bases away from the poly A tail of all kallikrein mRNAs (Table 3). With only one exception, all splice-junction sites are fully conserved among the human kallikrein genes (Table 3).



Chromosomal locus 19q13.3-q13.4

FIG. 1. An approximate 300-kb region of contiguous genomic sequence around chromosome 19q13.4. The direction of transcription of each gene is illustrated by *arrows*. *Boxes* represent genes and contain the gene names and their genomic length, in base pairs. Other commonly used names for these genes are also mentioned. Distances between genes in base pairs are shown between *boxes*. The Siglec and ACPT (testicular acid phosphatase) genes do not belong to the tissue kallikrein gene family. Figure is not drawn to scale. For full gene names, see Table 2 and abbreviation footnote.

V. Protein Homologies and Predicted Enzymatic Activity

The 15 members of the new human kallikrein gene family have been aligned to identify similarities (Fig. 3). Maximum homology between all these proteins is found around the catalytic amino acids histidine (with the conserved region

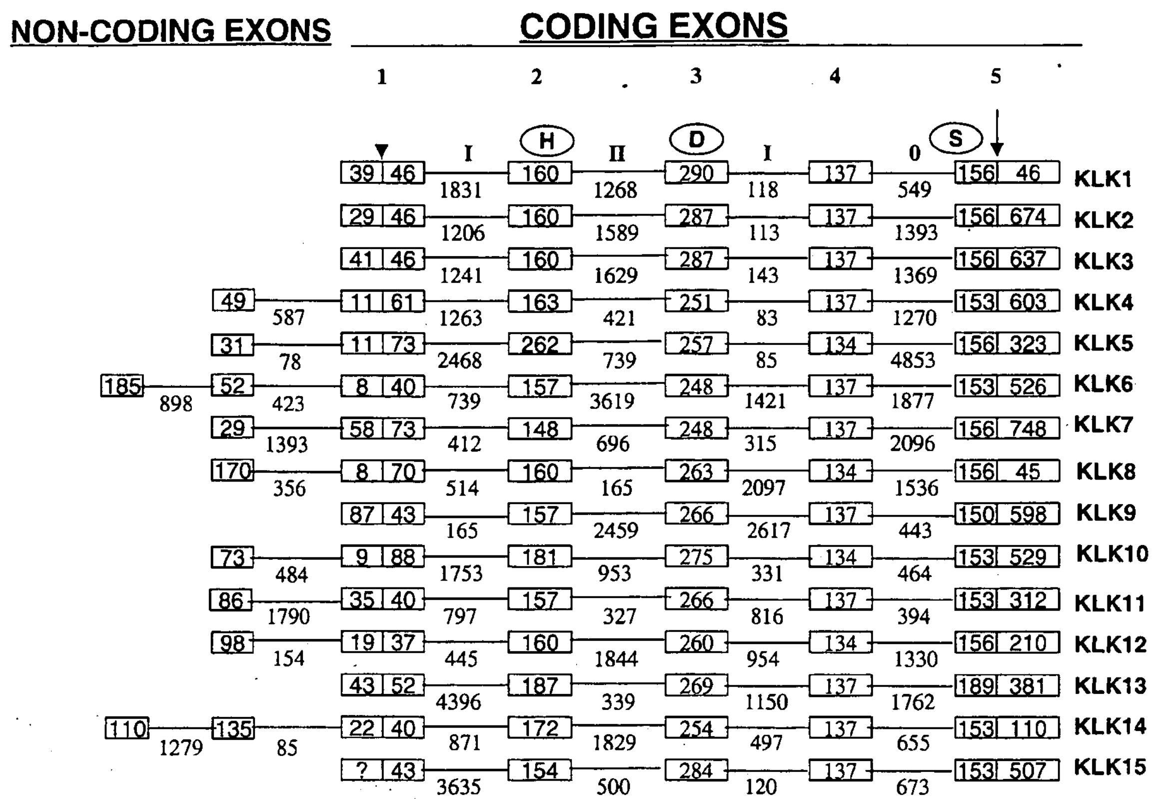


FIG. 2. Schematic diagram showing the comparison of the coding regions of the 15 kallikrein genes. Exons are shown by *solid bars* and introns by the *connecting lines*. *Letters above boxes* indicate relative positions of the catalytic triad that was found to be conserved in all genes; H, histidine; D, aspartic acid; and S, serine. *Roman numbers* indicate intron phases. The intron phase refers to the location of the intron within the codon; I denotes that the intron occurs after the first nucleotide of the codon; II, the intron occurs after the second nucleotide; 0, the intron occurs between codons. The intron phases are conserved in all genes. *Numbers inside boxes* indicate exon lengths and *numbers outside boxes* indicate intron lengths (in base pairs). The *arrowhead* represents the position of the start codon and the *arrow* indicates the position of the stop codon. *Question mark* denotes that region length is unknown. Figure is not drawn to scale.

TABLE 3. TATA, polyadenylation signals, and splice/junctions for the KLK genes[a]

Gene	TATA box	Polyadenylation signal[b]	Splice junctions
KLK1	TTTAAA (−21 bp)[c]	AGTAAA (−15 bp)	Fully conserved
KLK2	TTTATA (−35 bp)	AATAAA (−19 bp)	Fully conserved
KLK3	TTTATA (−22 bp)	AATAAA (−16 bp)	Fully conserved
KLK4	TTATAA (−30 bp)	AATAAA (−15 bp)	Fully conserved
KLK5	Not found	AATAAA (−8 to −11 bp)	Fully conserved
KLK6	Not found	AATAAA (−14 bp)	Fully conserved
KLK7	Not found	AATAAA (−16 bp)	Fully conserved
KLK8	Not found	AATAAA (−15 to −18 bp)	Fully conserved
KLK9	Not found	AGTAAA (−14 bp)	Fully conserved
KLK10	TTAAAA (−35 bp)	ACTAAA (−17 bp)	gc for gt at beginning of intron 4[d]
KLK11	Not found	AATAAA (−17 bp)	Fully conserved
KLK12	Not found	AATAAA (−16 bp)	Fully conserved
KLK13	Not found	TATAAA (−16 bp)	Fully conserved
KLK14	Not found	Putative AATAAA	Fully conserved
KLK15	Not found[e]	ATTAAA (−17 bp)	Fully conserved

[a] The information was derived from the GenBank entries shown in Table 2.
[b] Position of polyadenylation signal in base pairs before the poly-A tail.
[c] Denotes position of TATA box considering first nucleotide of start codon as 1.
[d] See Ref. 87.
[e] TATA box may be present in some genes for which the 5′-proximal promoter sequences have not as yet been accurately defined.

WVLTAA<u>H</u>C), aspartic acid (<u>D</u>LMLL), and serine (GD<u>S</u>G-GPL). In general, the amino acid identity between the various members of this family ranges from about 40–80%. The number and position of cysteine residues are highly conserved among the 15 human kallikreins and among other serine proteases. All members of this family possess between 10–12 cysteine residues, which are expected to form disulfide bridges. A number of other invariant amino acids (~25–30),

especially those around the active site of serine proteases, have been described (104). In the case of the human family of genes, there are 39 amino acids that are completely conserved among all 15 kallikreins (Fig. 3). Numerous other conservative amino acid substitutions are shown in Fig. 3. A phylogenetic tree of all human kallikreins and a few other serine proteases is shown in Fig. 4.

All proteins encoded by these genes are initially synthesized as preproenzymes that are then proteolytically processed to yield proenzymes by removal of the signal peptide, followed by activation (also by proteolysis) to the mature, enzymatically active forms. In Table 4, we present the reported signal and activation peptides as well as the length of the mature proteins that are encoded by these genes. It is important to mention that most of these cleavage sites have been predicted by computer programs and have been verified experimentally for only a few members.

The data of Table 4 suggest that most of the pro-forms of these enzymes are activated by cleavage at the carboxy-terminal end of either arginine (R) or lysine (K) residues (the preferred trypsin cleavage site). Since most of the human kallikrein enzymes have trypsin-like activity, they may potentially act as activating enzymes for either themselves (autoactivation) or other pro-forms of kallikreins. Kallikreins may participate in cascade pathways similar to those demonstrated for the digestive enzymes, coagulation, and apoptosis. These possibilities merit further investigation.

Protein sequence examination (Fig. 3) reveals that the three classical kallikreins possess an amino acid sequence of approximately 9–11 amino acids (the kallikrein loop) preceding the aspartic acid residue of serine proteases, which is not present in its entirety in any of the other 12 enzymes. This short sequence is thought to confer specificity for kininogenase activity but, as already mentioned, only hK1 is a potent kininogenase. KLK15 has a unique 8-amino acid sequence at positions 148–155, not found in any other kallikrein protein. Similarly, KLK13 possesses a unique amino-terminal and a unique carboxy-terminal end.

Serine proteases can be divided into two main evolutionary families, the trypsin-like serine proteases and the subtilisin-like pro-protein convertases, which presumably evolved through convergent evolution (105). The trypsin-like serine proteases are believed to have evolved from a single ancestral gene that duplicated in the course of evolution to give rise to other genes that have gradually mutated and evolved to related proteases and protease subfamilies with new functions. The various serine proteases can be markedly different in relation to their substrate specificity (106, 107). The differences are due to very subtle variations in the substrate binding pocket. Trypsin-like serine proteases have an aspartic acid in their binding pocket, which can form strong electrostatic bonds with arginine or lysine residues, which are usually present at the carboxyl-terminal part of the cleavage site. The important amino acid of the binding pocket, responsible for substrate specificity, is usually found six amino acids before the catalytic serine residue. From the 15 proteins aligned in Fig. 3, 11 have aspartic acid in this position and are expected to have trypsin-like activity. The four remaining enzymes, namely hK3 (has serine), hK7 (has asparagine), hK9 (has glycine), and hK15 (has glutamic acid), are expected to have chymotrypsin-like or other specific enzymatic activity (see also Table 4). The cleavage specificity of these enzymes needs to be established experimentally, with the exception of hK3, which has already been characterized (50).

VI. Hormonal Regulation of Kallikrein Genes

KLK1 expression has been studied in animals, and it was concluded, by using gene-specific probes, that this enzyme is not directly regulated by androgens either in the salivary glands or the kidney (31, 108–111). Similarly, no regulation of the KLK1 gene by thyroid hormones has been demonstrated (109–111). Results of KLK1 regulation by mineralocorticoids are inconclusive (112, 113). Other data support the transcriptional up-regulation of KLK1 by estrogens (114, 115) and by dopamine in rat pituitary (116). The demonstration that KLK1 expression in human endometrium is higher during the middle of the menstrual cycle is also suggestive of KLK1 up-regulation by estrogens in this tissue (117).

Murray *et al.* (19) have reported the presence of various motifs that are reminiscent of consensus estrogen-, progestin-, glucocorticoid-, or cAMP-response elements in the 5′-flanking sequence of the human KLK1 gene (19). However, these putative elements have not been functionally tested. Consequently, no conclusion can be drawn regarding direct regulation of KLK1 transcription by steroid or other hormones.

The regulation of the PSA (KLK3) gene by steroid hormones has been extensively studied. Initially, two androgen-response elements were identified in the proximal PSA promoter, at positions −170 [ARE1] and −394 (ARE2), respectively (118–120). These AREs have been functionally tested and found to be active in LNCaP prostate cancer cells. More recently, Schuur *et al.* have identified various regions of 5′-sequences of the PSA gene around −6 to −4 kb and demonstrated presence of a putative androgen-response element at position −4,136 (ARE3), which markedly affects PSA transcription upon induction by androgens (121). It was also demonstrated that this area harbors an enhancer that is contained within a 440-bp fragment (121, 122). The upstream enhancer, containing the putative ARE3, has a dramatic effect on PSA transcription, in comparison to the two AREs in the proximal promoter (122). The hormonal regulation of the PSA gene is not tissue specific since PSA has also been found to be regulated by steroid hormones *in vitro* and *in vivo* in breast tissues and breast carcinoma cell lines (123–125). Despite this, a number of investigators have used the PSA promoter and enhancer region to deliver and express therapeutic vectors to prostate tissue, in experimental gene therapy protocols (126–132).

A number of investigations have clearly demonstrated hormonal regulation of the PSA gene primarily by androgens in the prostatic carcinoma cell line LNCaP (133) and by androgens and progestins in the breast carcinoma cell lines BT-474, T-47D, and MFM223 (123, 125, 134).

The 5′-promoter sequences of the KLK2 gene have been studied by Murtha *et al.* (135) who have identified functional androgen response elements in the promoter of this gene.

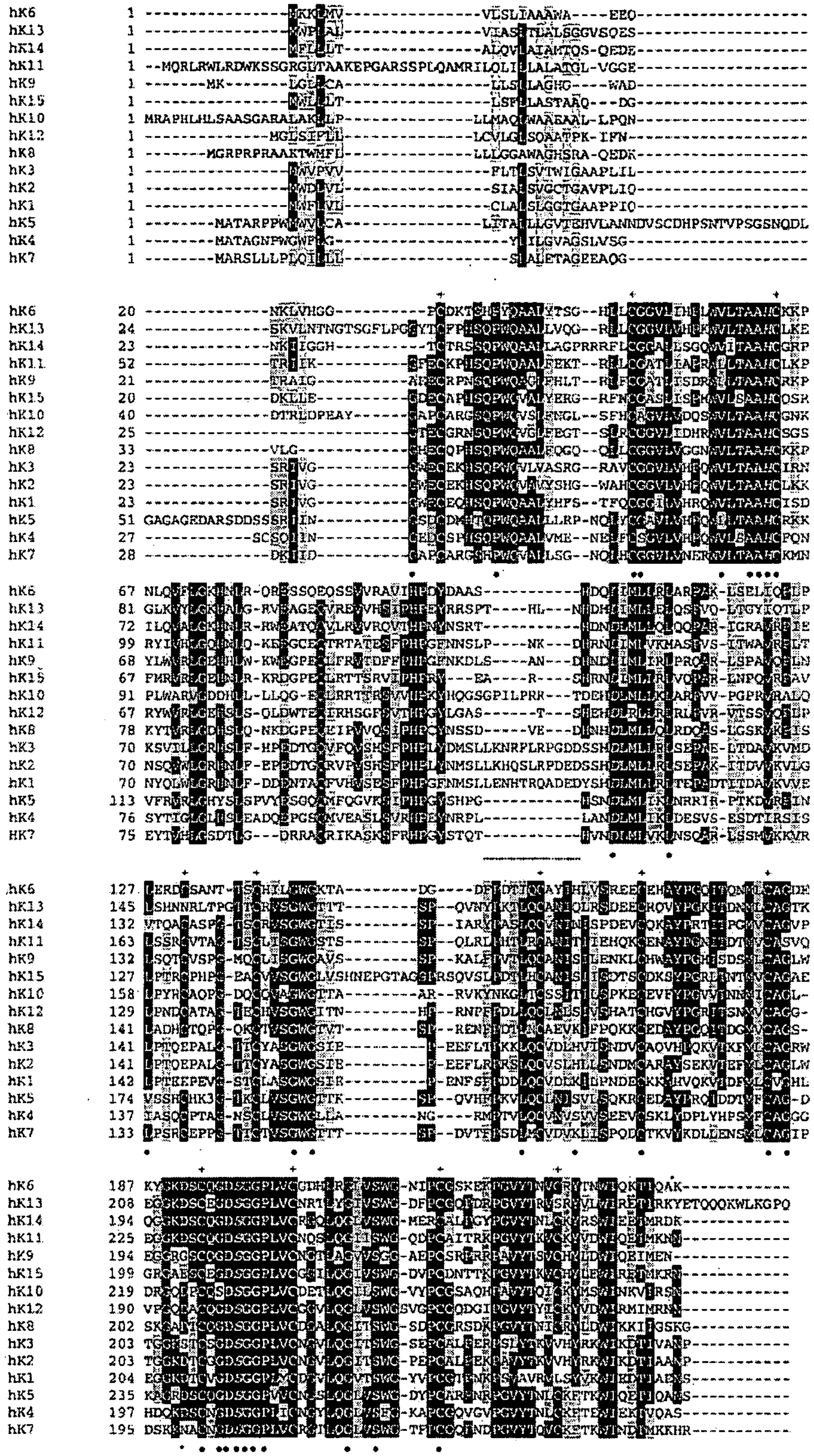


FIG. 3. Alignment of the deduced amino acid sequence of the 15 kallikrein proteins. *Dashes* represent gaps to bring the sequences to better alignment. The amino acids of the catalytic triad (H, D, S) are shown in *italics*. Identical amino acids are highlighted in *black* and similar residues in *gray*. The 29 invariant serine protease residues are marked by (●) on the *bottom*, and the cysteine residues by (+) on *top of each block*. The *dotted area* represents the kallikrein loop sequence. The *asterisk* denotes the position of the amino acid of the binding pocket that is crucial for substrate specificity (for trypsin-like enzymes the amino acid is D). For more details, see text.

The same group has subsequently shown that KLK2 is up-regulated by androgens and progestins in the breast carcinoma cell line T47-D (136) while Riegman *et al.* (137) showed up-regulation by androgens. More recently, it has been demonstrated that, similarly to PSA, a 5′-enhancer region exists about 3–5 kb upstream from the transcription site of the KLK2 gene (138). The enhancer region contains an androgen response element that was shown to be functionally active. Consistent with these data are the findings of hK2 protein secretion and up-regulation by androgens and progestins in

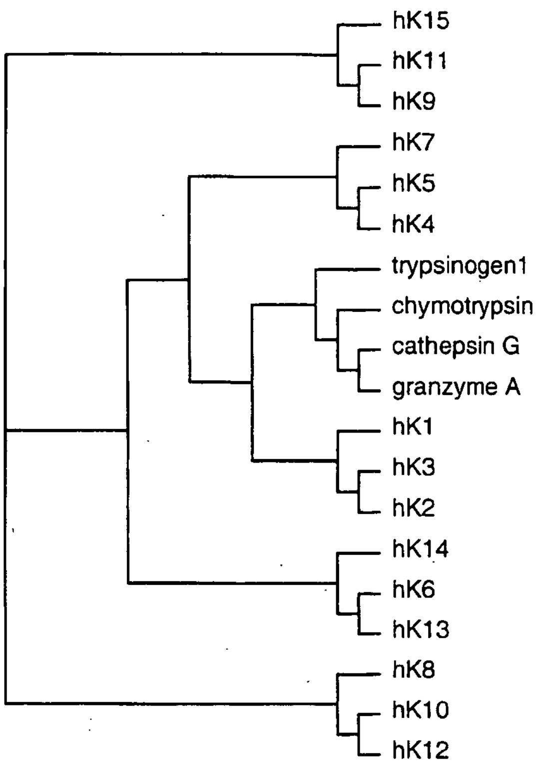


FIG. 4. Dendrogram of the predicted phylogenetic tree for the 15 kallikrein proteins and a few other related serine proteases. The neighbor-joining method was used to align these proteins. The classical kallikreins (hK1, hK2, and PSA) were grouped together; other kallikreins and serine proteases were separated in different groups, as shown. For full protein names, please see Table 2 and abbreviation footnote.

the breast cancer cell lines BT-474, T47-D, and MFM223 (134). Although the KLK2 gene promoter is not exclusively functional in the prostate, gene therapy protocols have used it for prostate cancer therapy (139).

The KLK4 gene was found to be up-regulated by androgens in the prostatic carcinoma cell line LNCaP (70) and by androgens and progestins in the breast carcinoma cell line BT-474 (71). The mode of regulation of KLK2 and KLK4 genes appears to be very similar to the mode of regulation of PSA (KLK3). Stephenson *et al.* (72) have identified putative androgen response elements in the proximal promoter region of the KLK4 gene (up to 553 bp from the transcription initiation site). However, such putative AREs have not been functionally tested, and no data have been published as yet on the characterization of possible enhancer regions further upstream from the proximal KLK4 promoter.

For the remaining 11 human kallikrein genes that have been recently identified, in none of them was the promoter functionally tested for the presence for hormone response elements (HREs). Most studies regarding hormonal regulation of these new genes have been performed with the breast carcinoma cell line BT-474 and, in some cases, with the prostatic carcinoma cell line LNCaP and other breast carcinoma cell lines. It is clear that for 10 of 11 genes under discussion (KLK5-KLK15), transcription is affected by steroid hormones, with the selectivities and potencies shown in Table 5. Most genes appear to be up-regulated by estrogens, androgens, and progestins but with different potencies. It is possible that some of these genes are hormonally regulated through indirect mechanisms, involving *trans*-acting elements (140).

Clearly, there is a need to functionally characterize the promoter and enhancer regions of these genes to understand better the mechanism of transcriptional and posttranscriptional regulation by steroid hormones.

VII. Tissue Expression of Kallikreins

KLK1 gene expression is highest in the pancreas, kidney, and salivary glands (9). The other two classical kallikrein genes, KLK3 and KLK2, were thought, for many years, to be expressed exclusively in the prostate (39–42, 46, 141, 142). By using highly sensitive immunological techniques (143), RT-PCR technology (144) as well as immunohistochemistry (145), it has now been demonstrated unequivocally that both KLK3 and KLK2 genes are expressed in diverse tissues but at relatively much lower concentrations than prostatic tissues (55–57, 146–148). Especially, hK3 (PSA) and hK2 proteins and mRNA have been found in significant amounts in the female breast and at lower levels in many other tissues (Table 6). KLK4 also appears to have prostatic-restricted expression (70) but by RT-PCR, it was demonstrated that it is also expressed in breast and other tissues (71, 72). None of the remaining kallikreins is tissue-specific, although certain genes are preferentially expressed in breast (*e.g.*, KLK5, KLK6, KLK10, KLK13), skin (KLK5, KLK7, KLK8), central nervous system (KLK6, KLK7, KLK8, KLK9,KLK14), salivary glands (almost all kallikreins), etc. A diagrammatic representation of expression of all these kallikreins in human tissues is shown in Fig. 5. Most data have been generated by RT-PCR.

It is clear that there is frequent coexpression of many kallikreins in the same tissues, and this may point to a functional relationship. For example, it has been shown that hK3 and hK2 are regulated by similar mechanisms (134) (see also previous section) and that they are frequently coexpressed in tissues and body fluids (146–148). *In vitro* data have demonstrated that hK2, which has trypsin-like activity, can activate the proform of PSA (149–151). Other functional relationships between members of the kallikrein gene family have not been demonstrated as yet.

VIII. Variants of Kallikrein Transcripts

A relatively large number of variant transcripts have already been identified for the classic and the new human kallikrein genes (Table 7). The functional and diagnostic importance of these transcripts has not as yet been studied in detail. It will be interesting to examine whether any of these transcripts are specific for certain disease states or tissues. Although other forms of some kallikreins in serum have already been described (*e.g.*, kallikreins bound to proteinase inhibitors, internally clipped kallikreins, circulating proforms, etc.), these will not be described in this review. Excellent accounts of these forms and their clinical signifi-

TABLE 4. Proteins encoded by kallikrein genes

Kallikrein	Length of pre-proenzyme	Length of signal peptide (cleavage)[a]	Length of activation peptide/cleavage[a]	Length of mature protein	Amino acid of substrate binding pocket	Reference
hK1	262	17 (A ↓ A)	7 (R ↓ I)	238	D	34, 35, 43, 49
hK2	261	17 (A ↓ V)	7 (R ↓ I)	237	D	43, 49, 94
hK3	261	17 (A ↓ A)	7 (R ↓ I)	237	S	43, 49, 95–97
hK4	254	26 (G ↓ S)	4 (Q ↓ I)	224	D	70–72
hK5	293	29 (A ↓ N)	37 (R ↓ I)	227	D	80, 81
hK6	244	16 (A ↓ E)	5 (K ↓ L)	223	D	73, 74, 82, 83
hK7	253	22 (G ↓ E)	7 (K ↓ I)	224	N	84, 85, 107
hK8	260	28 (A ↓ Q)	4 (K ↓ V)	228	D	86, 98
hK9	251	19 (A ↓ D)	3 (R ↓ A)	229	G	67
hK10	276	33 (A ↓ A)	9 (R ↓ L)	234	D	76
hK11	250	18 (G ↓ E)	3 (R ↓ I)	229	D	88, 89, 100
hK12	248	17 (A ↓ A)	4 (K ↓ I)	227	D	77
hK13	277	20 (S ↓ Q)	5 (K ↓ V)	252	D	78
hK14	251	18 (S ↓ Q)	6 (K ↓ I)	227	D	90
hK15	256	16 (A ↓ Q)	5 (K ↓ L)	235	E	69

[a] Most are predicted; need verification by experiment.

TABLE 5. Hormonal regulation of human kallikreins

Gene	Systems tested	HREs[a]	Functionally tested?	Up-regulating hormone(s)	Reference
KLK1	*In vivo* humans, rodents	Putative	No	Uncertain	19
KLK2	LNCaP; BT-474, T-47D	Yes (2 AREs)	Yes	Androgen, progestin	134–137
KLK3	LNCaP, BT-474, T-47D	Yes (3 AREs)	Yes	Androgen, progestin	118–125 133–134
KLK4	LNCaP; BT-474	Putative (AREs)	No	Androgen, progestin	70–72
KLK5	BT-474	NS (not studied)		Estrogen, progestin > androgen	80
KLK6	BT-474	NS		Estrogen, progestin > androgen	83
KLK7	BT-474	NS		Estrogen > glucocorticoid	85
KLK8	Not studied			–	
KLK9	BT-474	NS		Estrogen, progestin > androgen	67
KLK10	BT-474	Not found		Estrogen > androgen > progestin	140
KLK11	BT-474	NS		Estrogen, glucocorticoid	89
KLK12	LNCaP, BT-474, T-47D	NS		Androgen, progestin > estrogen but in BT-474, estrogen > androgen > progestin	77
KLK13	BT-474	NS		Androgen, progestin > estrogen	78
KLK14	Not studied				
KLK15	LNCaP		No	Androgen > progestin, estrogen	69

LNCaP, Prostate carcinoma cell line; BT-474, T-47D, breast carcinoma cell lines.
[a] Hormone response elements.

cance already exist (43, 47–49, 152–158). It should be emphasized that, in general, the putative proteins encoded by these variant transcripts have not been isolated. By open reading frame analysis, it has been predicted that most transcripts will produce truncated proteins due to frameshifts originating from deleted exons. More details on these variant transcripts and the predicted encoded proteins can be found in the literature cited in Table 7 (34, 69, 77, 78, 86, 94, 96–98, 137, 159–165).

IX. Association of Kallikreins with Human Diseases

As already mentioned, the only enzyme with efficient kininogenase activity, among the human kallikrein family members, is hK1. The biological effects of this enzyme, and of plasma kallikrein, are mediated mainly by kinin release. Kinin binds to specific G protein-coupled cell surface receptors to mediate diverse biological functions. The kallikrein-kinin system is involved in many disease processes, including inflammation (9), hypertension (166), renal disease (167, 168), pancreatitis (169), and cancer (170–174). A recent book summarizes elegantly the physiology, molecular biology, and pathophysiology of the kallikrein-kinin system and its association to various disease processes (175).

Among all other kallikreins, the best studied, by far, is PSA (hK3) and especially, its application to prostate cancer diagnostics. A comprehensive volume on PSA as a tumor marker has been recently published (176). The extensive literature on PSA and prostate cancer does not warrant further discussion in this review.

Although PSA concentration is generally elevated in the serum of prostate cancer patients, one less known and usually not well understood finding is PSA down-regulation in prostate cancer tissue, in comparison to normal or hyperplastic prostatic tissues (177–182). Furthermore, it has been demonstrated that lower tissue PSA concentration is associated with more aggressive forms of prostate cancer (182, 183). These data agree with those published for breast cancer, where it was found that PSA is down-regulated in cancerous breast tissues, in comparison to normal or hyperplastic breast tissues, and in more aggressive forms of breast cancer. Patients with PSA-positive tumors usually have earlier disease stage, live longer, and relapse less frequently (184–186). Furthermore, it was found that lower PSA levels in nipple as-

TABLE 6. Tissue expression of human kallikreins

Gene	Tissue expression[a]		Reference
	Highest	Other tissues	
KLK1	Pancreas, kidney, salivary glands	Sweat glands, intestine, CNS,[b] neutrophils, uterus, prostate, testis, breast, placenta	7, 9
KLK2	Prostate	Breast, thyroid, salivary glands	46, 147, 148
KLK3	Prostate	Breast, thyroid, salivary glands, lung, trachea	39–45, 54–57
KLK4	Prostate	Breast, thyroid, testis, uterus, adrenal, colon, spinal cord	70–72
KLK5	Breast, brain, testis, skin	Salivary glands, thymus, CNS, prostate, thyroid, trachea	80, 81
KLK6	CNS, breast, kidney, uterus	Salivary gland, spleen, testis	73, 74, 82, 83
KLK7	Skin, CNS, kidney, breast	Salivary glands, thymus, uterus, thyroid, placenta, trachea, testis, ovary	84, 85, 107
KLK8	CNS, skin, ovary		86, 98
KLK9	Thymus, testis, CNS, trachea	Breast, prostate, salivary glands, ovary, skin	67
KLK10	Breast, ovary, testis, prostate	Small intestine, lung, colon, pancreas, uterus, CNS, salivary glands, trachea	76
KLK11	Brain, skin, salivary gland, stomach, uterus, lung, thymus, prostate, spleen, liver, small intestine, trachea	Heart, fetal liver, breast, thyroid, skeletal muscle	88, 89
KLK12	Salivary glands, stomach, uterus, trachea, prostate, thymus, lung, colon, brain, breast, thyroid	Testis, pancreas, small intestine, spinal cord	77
KLK13	Breast, prostate, salivary glands, testis	Lung, heart, thymus, adrenal, colon, thyroid, trachea	78
KLK14	CNS	Breast, thyroid, uterus, thymus, colon, spleen, placenta, small intestine, kidney, bone marrow	90
KLK15	Thyroid, salivary glands, prostate	Adrenal, colon, testis, kidney	69

[a] Most data have been produced by RT-PCR technology.
[b] CNS, central nervous system.

pirate fluid of women are associated with higher risk for developing breast cancer (187). Other published data suggest that PSA may be a tumor suppressor (188), an inducer of apoptosis (188), a negative regulator of cell growth (189), and an inhibitor of angiogenesis (190, 191) and bone resorption (192, 193). These data have recently been reviewed (194).

Another set of investigations suggests that PSA may be associated with unfavorable prognosis/outcomes in breast, prostate, and other cancers. More specifically, it was found that breast tumors with higher PSA content do not respond well to tamoxifen therapy (195). Further, patients with breast tumors, which produce PSA after stimulation by medroxyprogesterone acetate (a synthetic progestin/androgen), have a worse prognosis than patients with tumors that do not produce PSA (196). A number of reports have indicated that PSA may cleave insulin-like growth factor binding protein-3, thus liberating insulin-like growth factor I (IGF-I), which is a mitogen for prostatic stromal and epithelial cells (197–199). PSA may activate latent transforming growth factor-β (TGFβ), stimulate cell detachment and facilitate tumor spread (200). Like other serine proteases, PSA may mediate proteolysis of basement membrane, leading to invasion and metastasis (201).

These confusing clinical data are due to differences in methodology, purity, and source of PSA preparations used, selection of patients, etc. Furthermore, the lack of knowledge of the biological pathways in which PSA is participating poses significant difficulties in interpreting these clinical observations, as further exemplified in a recent commentary (194).

Human glandular kallikrein 2 (hK2) appears to be a new, promising biomarker for prostatic carcinoma (43). It is clear that the diagnostic value of hK2 measurement in serum is not superior to PSA; hK2 may aid in the differential diagnosis between prostate cancer and benign prostatic hyperplasia (57–66) as well as in the identification of organ-confined *vs.* non-organ-confined disease (202). Immunohistochemical studies have shown that prostate cancer tissue produces more hK2 than normal or hyperplastic tissue (203, 204). However, recent quantitative data demonstrate that hK2 concentration, although to a lesser extent than PSA, is also decreased in cancerous tissue, in comparison to adjacent normal tissue (181). Although hK2 has been detected in breast and other tissues (146–148), no studies have as yet been performed to examine its biological action or its value as a breast disease biomarker.

Although it has been shown that KLK4 expression is relatively high in prostate (70, 71), there are no reports describing association or usefulness of this kallikrein in prostatic disease. It will be worthwhile to examine the possible clinical value of this kallikrein as a biomarker in prostatic and other diseases. Recently, KLK4 was found to be overexpressed in a subset of ovarian tumors (205).

A single report describes overexpression of KLK5 in ovarian carcinomas and association with less favorable clinical outcomes (206). Further, KLK6 appears to be dramatically down-regulated at metastatic breast cancer sites and up-regulated in a subset of primary breast and ovarian tumors (73). These data should be interpreted with caution since the number of patients was small and the techniques used were qualitative. Additionally, Little *et al.* (74) suggested that KLK6 may be amyloidogenic and may play a role in the development of Alzheimer's disease by cleaving amyloid precursor proteins. Recently, a number of newly cloned aspartyl proteinases were also shown to be amyloidogenic (207). The connection between various types of proteases and

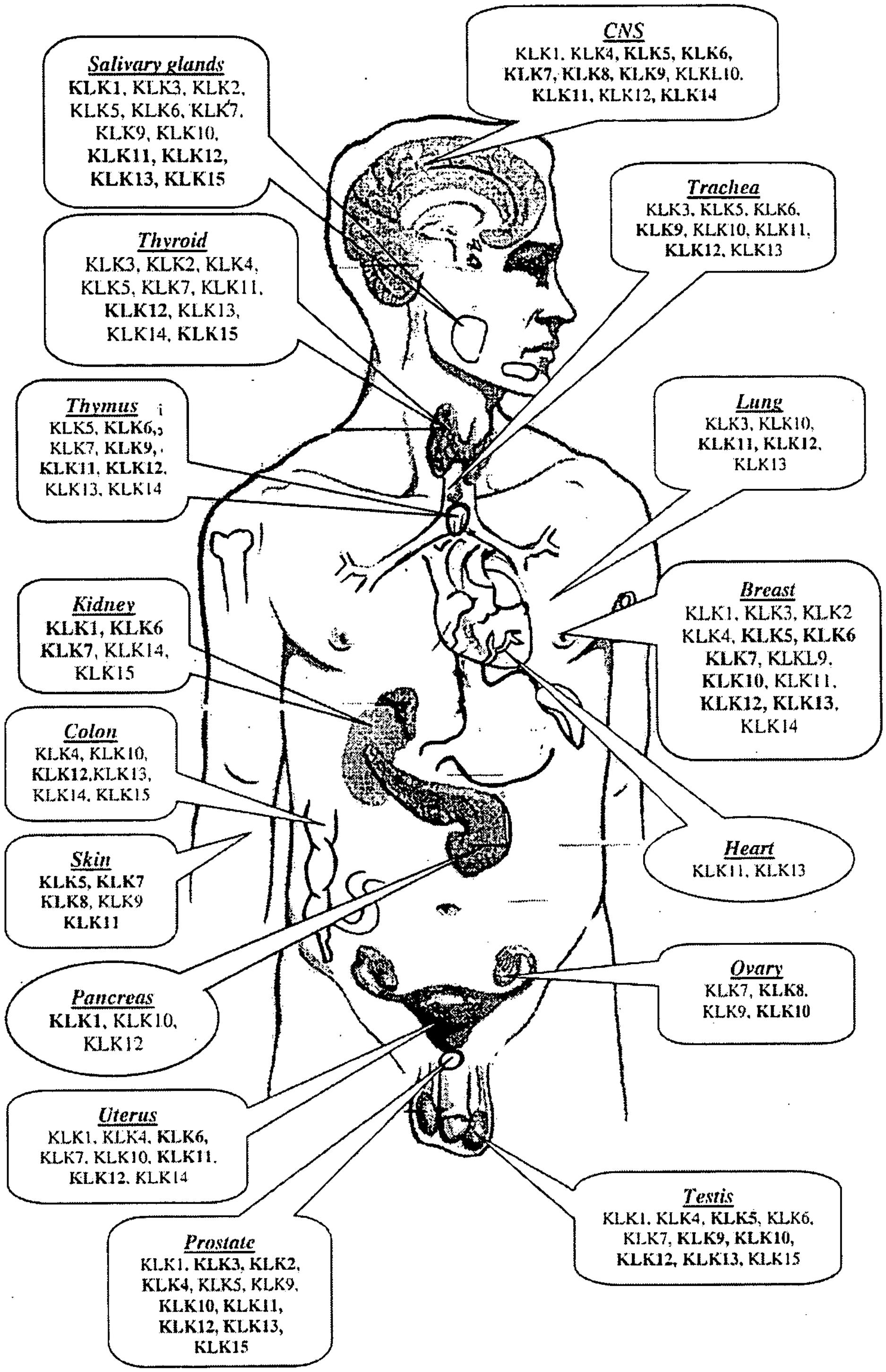


FIG. 5. Schematic representation of tissue kallikrein expression in various tissues. Higher level of expression is shown in *bold*. For more information and discussion, see text and Table 6.

this disease is still ill-defined. The connections of KLK7 with skin diseases, including pathological keratinization and psoriasis, have already been reported (75, 208). KLK7 was also found to be overexpressed in a subset of ovarian carcinomas (107). There are reports describing connection of KLK8 expression with diseases of the central nervous system, including epilepsy (209–212), injury (213, 214), and learning disturbances (215). Another report describes KLK8 overexpression in a subset of ovarian carcinomas (98). Although KLK10 has been shown to be a breast cancer tumor suppressor in animal models (76, 99), there is no report as yet describing prognostic or diagnostic value of KLK10 in breast carcinomas. Recently, KLK10 was found to be down-regulated in more aggressive forms of prostate cancer (216). Preliminary data suggest that KLK12, KLK13, and KLK14 may be down-regulated in a subset of breast carcinomas (77, 78,

90) while KLK15 may be overexpressed in more aggressive forms of prostate cancer (69).

The associations of kallikreins to human diseases are summarized in Table 8. Clearly, except for hK1, hK2, and hK3, the literature is quite limited and the value of the new kallikreins as disease biomarkers is just starting to be examined. Since most studies thus far used small numbers of clinical samples and qualitative methodologies, the data should be interpreted with caution. The knowledge that these kallikreins are secreted proteins supports the idea that they likely circulate in blood and that their concentration may be altered in certain human diseases, including cancer. The experience with hK3 (PSA) and hK2 in prostate cancer may be used to exploit other cancers, including those of breast, ovarian, lung, etc. These possibilities deserve further investigation.

TABLE 7. Variant transcripts of human kallikreins

Gene	No. of known variant transcripts	GenBank accession no.	References
KLK1	3	Not available (N/A)	34, 159, 160
KLK2	6	AF188746	94, 137, 161
KLK3	5	M21896 M21897	96, 97, 162, 163
KLK4	2	N/A	Our unpublished data[a]
KLK7	4	AF166330	85
KLK8	5	AB010780 AF095743 AF251125	86, 98, 164
KLK11	2	AF164623 AB041036	89, 100
KLK12	3	AF135025	77
KLK13	7	AF135024	78, 165
KLK15	3	AF242195	69

[a] Also, J. Clements, personal communication.

TABLE 8. Association of kallikreins to human disease

	Disease	Effect/use	Reference
KLK1	Inflammation; sepsis; pancreatitis; bone metabolism; heart disease; renal disease; cancer	Mediation by bradykinin or lysyl-bradykinin	9, 166–178
KLK2	Prostate cancer	Biomarker for diagnosis, monitoring, prognosis	43, 57–66, 202
	Breast cancer	Expressed in breast cancer but prognostic/diagnostic value not as yet examined	146–148
KLK3	Prostate cancer	Biomarker for diagnosis and monitoring	42–53
		Inducer of apoptosis; decreases cell proliferation; inhibitor of angiogenesis	188–191
	Breast cancer	Favorable prognostic indicator; down-regulated in more aggressive disease	184–187
KLK4	Ovarian cancer	Overexpression in a subset of more aggressive ovarian tumors	205
KLK5	Ovarian cancer	Overexpression in a subset of more aggressive ovarian tumors	206
KLK6	Breast cancer	Down-regulation at metastatic sites and up-regulation in a subset of primary tumors	73
	Ovarian cancer	Up-regulation in a subset of ovarian tumors	73
	Alzheimer's disease	Has amyloidogenic potential	74
KLK7	Pathological keratinization	Overexpression in lichen planus and benign oval keratosis	208
	Psoriasis	Overexpression	75
	Ovarian cancer	Overexpression; may be involved in tumor growth and metastasis	107
KLK8	CNS injury	Increased KLK8 expression	213, 214
	Kindling epilepsy	Increased KLK8 expression	209–212
	Ovarian cancer	Overexpression in a subset of tumors	98
KLK10	Breast cancer	Down-regulation; KLK10 may be a tumor suppressor	76, 99
	Prostate cancer	Down-regulated in more aggressive prostate cancer	216
KLK12	Breast cancer	Down-regulated in a subset of breast tumors	77
KLK13	Breast cancer	Down-regulated in a subset of breast and testicular tumors	78
KLK14	Breast cancer	Down-regulation	90
KLK15	Prostate cancer	Overexpressed in more aggressive forms	69

X. Physiological Functions

Among the 15 new human kallikrein genes, only 3 have been assigned to a specific biological function (Fig. 6). hK1 exerts its biological activity mainly through the release of lysyl-bradykinin (kallidin) from low molecular weight kininogen. However, the diverse expression pattern of hK1 has led to the suggestion that the functional role of this enzyme may be specific to different cell types (7, 22). Apart from its kininogenase activity, tissue kallikrein has been implicated in the processing of growth factors and peptide hormones (217–220) in light of its presence in pituitary, pancreas, and other tissues. As summarized by Bhoola *et al.* (7), hK1 has been shown to cleave pro-insulin, low density lipoprotein, the precursor of atrial natriuretic factor, prorenin, vasoactive intestinal peptide, procollagenase, and angiotensinogen. Kallikreins, in each cell type, may possess single or multiple functions, common or unique, but Bhoola *et al.* (7) suggest that the release of kinin should still be considered the primary effect of hK1 (7).

The physiological function of hK2 protein has been examined only recently, with the availability of preparations of recombinant origin, which are essentially free of hK3 (PSA)

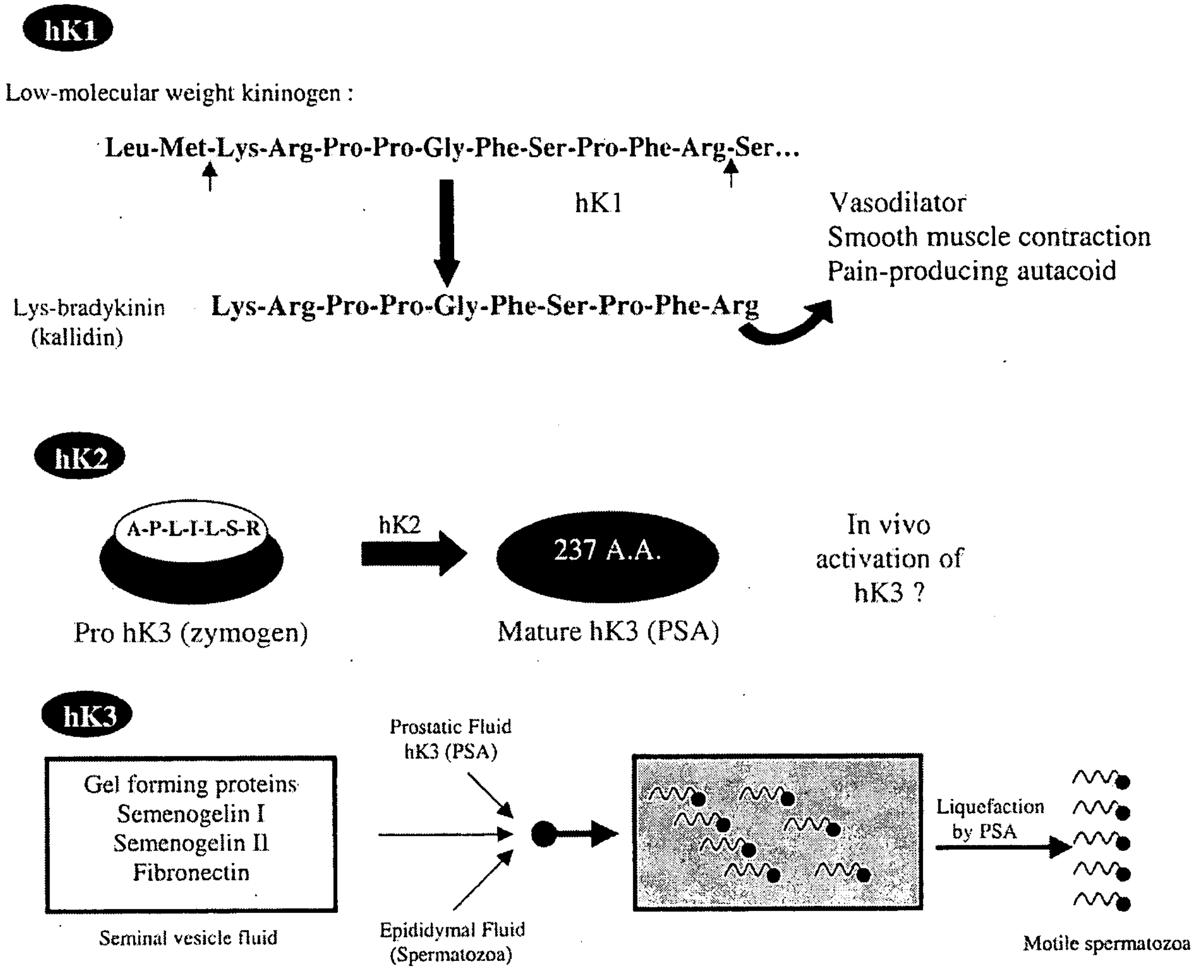


FIG. 6. Biological functions of the three classical kallikreins. hK1 cleaves low molecular weight kininogen and releases lysyl-bradykinin which mediates pleiotropic effects. Human glandular kallikrein 2 activates the pro-form of PSA. Other possible biological functions and substrates of hK2 are described in the text. hK3 (PSA) cleaves semenogelins and fibronectin and mediates seminal clot liquefaction, which increases the motility of spermatozoa. [Adapted with permission from H. G. Rittenhouse *et al.*: *Crit Rev Clin Lab Sci* 35:275–368, 1998 (43). © CRC Press.]

or other kallikrein contaminations (221–224). Three independent groups have reported activation of the pro-form of PSA by hK2 (Fig. 6) (149–151) with a process that is very similar to the autoactivation of hK2 (removal of 7 amino acids) (225). The study of substrate specificities between hK1 and hK2 reveals important differences (106, 226) suggesting that the two proteins have different natural substrates, a notion that is supported by the finding of very low kininogenase activity of hK2 in comparison to hK1 (14, 15). Seminal plasma hK2 was found to be able to cleave seminogelin I and seminogelin II but at different cleavage sites and at a lower efficiency than PSA (227). Since the amount of hK2 in seminal plasma is much lower than PSA (1–5%), the contribution of hK2 in the process of seminal clot liquefaction is expected to be relatively small (43).

In any biological fluid thus far studied, hK3 (PSA) and hK2 were found to coexist (146–148), suggesting a possible functional relationship along the lines described above. Furthermore, a role of hK2 in regulating growth factors, through IGFBP-3 proteolysis, has been suggested (228).

Recently, hK2 was found to activate the zymogen or single-chain form of urokinase-type plasminogen activator (uPA) *in vitro* (229). Since uPA has been implicated in the promotion of cancer metastasis, hK2 may be part of this pathway in prostate cancer.

While both hK1 and hK2 have trypsin-like enzymatic activities, hK3 has chymotrypsin-like substrate specificity (230–233). Since PSA is present at very high levels in seminal plasma, most studies focused on its biological activity within this fluid. Lilja (234) has shown that PSA hydrolyzes rapidly both seminogelin I and seminogelin II, as well as fibronectin, resulting in liquefaction of the seminal plasma clot after ejaculation (234) (Fig. 6). Several other potential substrates for PSA have been identified, including IGFBP-3 (197, 199), TGFβ (200), basement membrane (201), PTH-related peptide (192, 193), and plasminogen (191). The physiological relevance of these findings is still not clear.

hK3 is now known to be found at relatively high levels in nipple aspirate fluid (187, 235), breast cyst fluid (236–240), milk of lactating women (241), amniotic fluid (242), and tumor extracts (184–186). It is thus very likely that hK3 has biological extraprostatic functions in breast and other tissues

TABLE 9. Future directions in kallikrein research

Physiology	Identification of physiological substrates and metabolic pathways in various tissues Delineate mode of regulation—functional characterization of gene promoters Mode of activation and participation in cascade pathways Secretion and deactivation; binding to proteinase inhibitors/serpins Characterization and physiology of enzyme isoforms in different tissues
Pathobiology	Differential expression (overexpression/underexpression) between normal and diseased tissue Tumor promotion/metastasis or tumor suppressor activity Aberrant/ectopic expression, mutation. Activation or inactivation of other effector molecules (growth factors; peptide hormones; cytokines)
Diagnostics	Development of analytical tools (highly sensitive and specific immunoassays) Measurement in biological fluids (especially serum or plasma) Diagnosis; monitoring; prognosis; prediction of therapeutic response; population screening Tumor localization
Therapeutics	Overexpression; underexpression by using external modulators (*e.g.*, steroid hormone agonists/antagonists Serine protease inhibitors; activators Immunotherapy; vaccination Tissue-specific delivery of therapeutic agents by using gene promoters

and may also play a role during fetal development (243). These possibilities merit further investigation.

Among all other human kallikreins, some have been connected to physiological processes and pathological conditions (as described in *Section IX*) but none has been assigned to cleave a specific substrate. Human kallikrein enzymes, with the exception of hK1, hK2, and hK3, are not commercially available and the study of their biological function has not as yet been published. Below, we will attempt to formulate some functional hypotheses for the human kallikreins.

First, all kallikreins are predicted to be secreted proteases, and it is very likely that their biological function is related to their ability to digest one or more substrates. The diversity of expression in human tissues further suggests that they may act on different substrates in different tissues. Their enzymatic activity may initiate, by activation, or terminate, by inactivation, events mediated by other molecules, including hormones, growth factors, receptors, and cytokines. The parallel expression of many kallikreins in the same tissues further suggests that they may participate in cascade reactions similar to those established for the processes of digestion, fibrinolysis, coagulation, and apoptosis. The role of these enzymes in tumor metastasis, as suggested for other proteases (244, 245), should be further investigated.

XI. Future Directions

In Table 9, we summarize some areas that may be fruitful for future kallikrein research. We have already indicated that it will be important to identify the physiological substrates of these enzymes in different tissues and the metabolic pathways in which they participate. The mode of hormonal regulation has been extensively studied only for KLK3 and KLK2. It will be important to functionally characterize gene promoters in view of the preliminary knowledge that the expression of most of these proteases in breast and prostate cancer cell lines is affected by steroid hormones. In addition, the details of activation and deactivation of these enzymes are still obscure. For some of these genes, we already have some information regarding differential expression between normal and diseased tissues. More data are needed. The possible mutational spectrum of these genes in cancer has not been examined.

The most successful clinical application of hK3 (PSA) is currently in the diagnosis and monitoring of prostate cancer. It is anticipated that all these serine proteases circulate in the peripheral blood since they are secreted proteins. It will be important to develop the tools necessary to allow specific and highly sensitive detection of these proteins in biological fluids. Once these tools are available, we should examine whether any of these enzymes have value for diagnosis, monitoring, prediction of therapeutic response, and population screening for diseases such as prostate, breast, ovarian, and other cancers. Applicability to nonmalignant diseases, *e.g.*, Alzheimer's disease, skin pathologies, and inflammatory, autoimmune, and other chronic diseases of many organs in which kallikreins are expressed, should also be examined. Some of these enzymes may be useful targets for tumor localization with specific binding reagents or for therapeutic interventions. If any of these enzymes are shown to participate in cancer metastasis, it may be useful to examine proteinase inhibitors for therapeutic applications. Other possibilities include the use of some of these genes and their promoters for tissue-specific delivery of gene therapy or for over- or underexpression, using exogenously administered modulators (*e.g.*, hormones or hormone blockers) that are known to affect their expression.

XII. Conclusions

In this review, we attempted to summarize the very latest progress in research related to the human kallikrein gene family. For many years, this family was thought to consist of only three genes. We have provided strong evidence suggesting that the human kallikrein gene family now includes at least 15 genes, which are tandemly localized on chromosome 19q13.4 and have significant similarities at both the gene and protein level. Genomic analysis of a large region around the human kallikrein gene locus allowed not only the

precise mapping of these genes but also the delineation of the genomic organization, the prediction of protein sequence and structure, the construction of phylogenetic trees, and the comparison of homologies between all human kallikreins. The diverse tissue expression patterns and the parallel expression of many kallikreins in the same tissues suggest multiple physiological roles as well as possible interactions between the kallikrein enzymes. Many fruitful avenues of investigation are now possible. Most kallikrein genes are regulated by steroid hormones. Protein sequence variation among the kallikreins suggests that each one of them interacts with a specific substrate or a very restricted number of substrates to mediate specific biological events. Much needs to be learned about the substrate specificity of these kallikreins in diverse tissues and the mediation of biological effects from their enzymatic action.

The human kallikrein gene family has contributed the best tumor marker ever developed (PSA). It is possible that other kallikrein members may have applicability as biomarkers in cancer and other chronic and acute diseases. Unfortunately, no methods currently exist to monitor the newly discovered kallikreins with high sensitivity and specificity. The emergence of these new technologies may eventually lead to novel clinical applications of kallikreins other than PSA. We hope that this update will facilitate new developments in this field and lead to practical applications in diverse human diseases.

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Note Added in Proof

Since preparation of this review, a few important developments have occurred as follows: The publication of a draft form of the sequence of the human genome will facilitate further genomic analysis within and around the human kallikrein gene locus. A recent paper further summarizes tissue expression data of kallikreins by array analysis (246). Highly sensitive and specific immunoassays for hK6 (247) and hK10 (248) have been published. With these methods, it was found that hK6 may be a biomarker for Alzheimer's disease (249) and a circulating tumor marker for ovarian cancer (250) and that hK10 is a promising new serum tumor marker for ovarian cancer (251).

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EXHIBIT C: Comparison of active site homology with PVP and kallkrein/protease proteins

1. Kallikrein 6 – [Rattus norvegicus]

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>gi|9506997|ref|NP_062048.1|  G  kallikrein 6 [Rattus norvegicus]
 gi|2853366|gb|AAC02300.1|  G  myelencephalon specific protease [Rattus
norvegicus]
          Length = 251

 Score =  492 bits (1266), Expect = e-138
 Identities = 223/251 (88%), Positives = 241/251 (96%)

Query: 1   MPMKMLTMKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLID 60
            MP KMLT+K LALCL+LAKSAWSE+Q+KVVHGGPCLK+SHPFQAALYTSGHLLCGGVL+
Sbjct: 1   MPTKMLTVKTLALCLILAKSAWSEDQDKVVHGGPCLKNSHPFQAALYTSGHLLCGGVLVG 60
              Histidine motif
Query: 61  PQWVLTAAHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLK 120
            PQWVLTAAHCKKPNL+V LGKHNLRQTETFQRQISVDRTIVHPRYNP+THDNDIMMVHLK
Sbjct: 61  PQWVLTAAHCKKPNLEVYLGKHNLRQTETFQRQISVDRTIVHPRYNPQTHDNDIMMVHLK 120

Query: 121 NPVKFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDFPDTIQCADVHLVPREQCERAYP 180
             PVKFS++IQPLPLK DCSE+NP+CQILGWGKMENG+FPDTIQCADV LV RE+CERAYP
Sbjct: 121 RPVKFSQRIQPLPLKKDCSEKNPDCQILGWGKMENGEFPDTIQCADVQLVSREECERAYP 180
                                  Serine motif
Query: 181 GKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTH 240
            GKIT+SMVCAGD +EGNDSCQGDSGGPLVCGG LRG+VSWGDMPCGSKEKPGVYTDVCTH
Sbjct: 181 GKITRSMVCAGDKREGNDSCQGDSGGPLVCGGHLRGIVSWGDMPCGSKEKPGVYTDVCTH 240

Query: 241 IRWIQNILRNK 251
            IRWIQNI+RNK
Sbjct: 241 IRWIQNIIRNK 251
```

NOTE: Query – represents PVP protein query sequence
Subject – represents the comparison protein

U.S. Ser. No. 09/486,247
Exhibit C

2. Kallikrein 8, isoform 2 [Homo sapiens]

```
>gi|21464127|ref|NP_653088.1|  kallikrein 8 isoform 2 [Homo sapiens]
 gi|5672479|dbj|BAA82666.1|  neuropsin type2 [Homo sapiens]
         Length = 305

 Score =  238 bits (608), Expect = 8e-62
 Identities = 108/232 (46%), Positives = 158/232 (68%), Gaps = 6/232 (2%)
                                                 Histidine motif
Query: 25  EQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAHCKKPNLQVILGKHNL 84
           +++KV+ G  C   S P+QAAL+    LLCGGVL+   WVLTAAHCKKP   V LG H+L
Sbjct: 74  QEDKVLGGHECQPHSQPWQAALFQGQQLLCGGVLVGGNWVLTAAHCKKPKYTVRLGDHSL 133

Query: 85  RQTETFQRQISVDRTIVHPRYNP---ETHDNDIMMVHLKNPVKFSKKIQPLPLKNDCSEE 141
           +  +  +++I V ++I HP YN    E H++D+M++ L++      K++P+ L + C++
Sbjct: 134 QNKDGPEQEIPVVQSIPHPCYNSSDVEDHNHDLMLLQLRDQASLGSKVKPISLADHCTQP 193

Query: 142 NPNCQILGWGKMENG--DFPDTIQCADVHLVPREQCERAYPGKITQSMVCAGDMKEGNDS 199
              C + GWG + +   +FPDT+ CA+V + P+++CE AYPG+IT  MVCAG  K G D+
Sbjct: 194 GQKCTVSGWGTVTSPRENFPDTLNCAEVKIFPQKKCEDAYPGQITDGMVCAGSSK-GADT 252
        Serine motif
Query: 200 CQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRNK 251
           CQGDSGGPLVC G L+G+ SWG  PCG  +KPGVYT++C ++ WI+ I+ +K
Sbjct: 253 CQGDSGGPLVCDGALQGITSWGSDPCGRSDKPGVYTNICRYLDWIKKIIGSK 304
```

3. Kallikrein 14 preproprotein [Homo sapiens]

```
>gi|11545747|ref|NP_071329.1|  kallikrein 14 preproprotein [Homo sapiens]
 gi|6715552|gb|AAD50773.2|  kallikrein-like protein 6 [Homo sapiens]
 gi|13897995|gb|AAK48524.1|  kallikrein 14 [Homo sapiens]
 gi|13897993|gb|AAK48523.1|  kallikrein 14 [Homo sapiens]
 gi|10799399|gb|AAG23260.1|  Homo sapiens kallikrein-like protein 6
 gi|12230294|sp|Q9P0G3|KLK14_HUMAN  Kallikrein 14 precursor (Kallikrein-like
protein 6) (KLK-L6)
          Length = 251

 Score =  238 bits (606), Expect = 1e-61
 Identities = 107/241 (44%), Positives = 156/241 (64%), Gaps = 4/241 (1%)
                                                                 Histidine motif
Query: 15  LVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGH--LLCGGVLIDPQWVLTAAHCKK 72
           L +A +    E++ K++ G  C + S P+QAAL        LCGG L+  QWV+TAAHC +
Sbjct: 11  LAIAMTQSQEDENKIIGGHTCTRSSQPWQAALLAGPRRRFLCGGALLSGQWVITAAHCGR 70
                                                     Aspartic acid motif
Query: 73  PNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKIQPL 132
           P LQV LGKHNLR+ E  Q+ + V R + HP YN  THDND+M++ L+ P +  + ++P+
Sbjct: 71  PILQVALGKHNLRRWEATQQVLRVVRQVTHPNYNSRTHDNDLMLLQLQQPARIGRAVRPI 130

Query: 133 PLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKITQSMVCA 190
            +   C+    +C++ GWG + +    +P ++QC ++++ P E C++AYP IT  MVCA
Sbjct: 131 EVTQACASPGTSCRVSGWGTISSPIARYPASLQCVNINISPDEVCQKAYPRTITPGMVCA 190
                     Serine motif
Query: 191 GDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRWIQNILRN 250
           G  + G DSCQGDSGGPLVC G+L+GLVSWG   C      PGVYT++C +  WI+  +R+
Sbjct: 191 GVPQGGKDSCQGDSGGPLVCRGQLQGLVSWGMERCALPGYPGVYTNLCKYRSWIEETMRD 250

Query: 251 K 251
           K
Sbjct: 251 K 251
```

U.S. Ser. No. 09/486,247
Exhibit C

4. KLK (kallikrein) 15 [Saguinus oedipus]

```
>gi|42759849|gb|AAS45302.1|   KLK15 [Saguinus oedipus]
         Length = 255

 Score =  221 bits (564), Expect = 1e-56
 Identities = 100/252 (39%), Positives = 154/252 (61%), Gaps = 14/252 (5%)
                                                           Histidine motif
Query: 10   MLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAAH 69
            +L L  +L  +A  ++  K++ G  C   S P+Q ALY  G   CG  LI P WVL+AAH
Sbjct: 4    LLPLSFLLTSTA--QDGGKLLEGEECAPHSQPWQVALYERGRFNCGASLISPHWVLSAAH 61
                                                   Aspartic acid motif
Query: 70   CKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNPETHDNDIMMVHLKNPVKFSKKI 129
            C+    ++V LG+HNLR+ +  ++  +  R I HPRY   +H +DIM++ L  P + + ++
Sbjct: 62   CQSRFMRVRLGEHNLRKRDGPEQLRTASRVIPHPRYEARSHRHDIMLLRLVQPARLTPQV 121

Query: 130  QPLPLKNDCSEENPNCQILGWGKMENGD------------FPDTIQCADVHLVPREQCER 177
            +P+ L   C    C + GWG + + +             PDT+ CA++ ++   C++
Sbjct: 122  RPVVLPTRCPHPGEACVVSGWGLVSHNEPGTTGRPQSQVSLPDTLHCANISIISDASCDK 181
                                         Serine motif
Query: 178  AYPGKITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDV 237
             YPG++T +MVCAG    G +SC+GDSGGPLVCGG L+G+VSWGD+PC +  KPGVYT V
Sbjct: 182  NYPGRLTNTMVCAGAEGRGAESCEGDSGGPLVCGGILQGIVSWGDVPCDNTTKPGVYTKV 241

Query: 238  CTHIRWIQNILR 249
            C +++WI+ ++
Sbjct: 242  CRYVKWIRETMK 253
```

U.S. Ser. No. 09/486,247
Exhibit C

5. Kallikrein 11 isoform 2 precursor [Homo sapiens]

```
>gi|21618357|ref|NP_659196.1|  kallikrein 11 isoform 2 precursor [Homo
sapiens]
 gi|3649791|dbj|BAA33404.1|  serine protease (TLSP) [Homo sapiens]
 gi|8574439|dbj|BAA96797.1|  prostate-type hippostasin [Homo sapiens]
          Length = 282

 Score =  221 bits (563), Expect = 1e-56
 Identities = 104/249 (41%), Positives = 151/249 (60%), Gaps = 6/249 (2%)
                                                             Histidine motif
Query: 8    MKMLALCLVLAKSAWSEEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTA 67
            M++L L L+    +       + +++ G  C    S P+QAAL+     LLCG  LI P+W+LTA
Sbjct: 33   MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTA 92
                                                          Aspartic acid motif
Query: 68   AHCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRYNP----ETHDNDIMMVHLKNPV 123
            AHC KP    V LG+HNL++ E  ++  +    +  HP +N     + H NDIM+V + +PV
Sbjct: 93   AHCLKPRYIVHLGQHNLQKEEGCEQTRTATESFPHPGFNNSLPNKDHRNDIMLVKMASPV 152

Query: 124  KFSKKIQPLPLKNDCSEENPNCQILGWGKMENGDF--PDTIQCADVHLVPREQCERAYPG 181
             +  ++PL  L + C      +C I GWG   +     P T++CA++ ++  ++CE AYPG
Sbjct: 153  SITWAVRPLTLSSRCVTAGTSCLISGWGSTSSPQLRLPHTLRCANITIIEHQKCENAYPG 212
                                   Serine motif
Query: 182  KITQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHI 241
             IT +MVCA   + G DSCQGDSGGPLVC    L+G++SWG   PC    KPGVYT VC ++
Sbjct: 213  NITDTMVCASVQEGGKDSCQGDSGGPLVCNQSLQGIISWGQDPCAITRKPGVYTKVCKYV 272

Query: 242  RWIQNILRN 250
             WIQ  ++N
Sbjct: 273  DWIQETMKN 281
```

U.S. Ser. No. 09/486,247
Exhibit C

6. Serine protease [Rattus rattus]

```
>gi|3559978|emb|CAA06643.1|   serine protease [Rattus rattus]
 gi|6093538|sp|O88780|NRPN_RAT   Neuropsin precursor (NP) (Kallikrein 8) (Brain
serine protease 1)
          Length = 260

 Score =  233 bits (594), Expect = 4e-60
 Identities = 110/245 (44%), Positives = 155/245 (63%), Gaps = 10/245 (4%)
                                                             Histidine motif
Query: 13  LCLVLAKSAWS----EEQEKVVHGGPCLKDSHPFQAALYTSGHLLCGGVLIDPQWVLTAA 68
            + L L   AW+     +  K++ G  C   S P+Q AL+    L+CGGVL+  +WVLTAA
Sbjct: 13  ILLFLLMGAWAGLTRAQGSKILEGQECKPHSQPWQTALFQGERLVCGGVLVGDRWVLTAA 72
                                                     Aspartic acid motif
Query: 69  HCKKPNLQVILGKHNLRQTETFQRQISVDRTIVHPRY---NPETHDNDIMMVHLKNPVKF 125
            HCKK    V LG H+L++ +  +++I V R+I HP +   NPE H +DIM++ L+N
Sbjct: 73  HCKKDKYSVRLGDHSLQKRDEPEQEIQVARSIQHPCFNSSNPEDHSHDIMLIRLQNSANL 132

Query: 126 SKKIQPLPLKNDCSEENPNCQILGWGKMEN--GDFPDTIQCADVHLVPREQCERAYPGKI 183
              K++P+ L N C +    C I GWG + +   +FP+T+ CA+V +  + +CERAYPGKI
Sbjct: 133 GDKVKPIELANLCPKVGQKCIISGWGTVTSPQENFPNTLNCAEVKIYSQNKCERAYPGKI 192
                          Serine motif
Query: 184 TQSMVCAGDMKEGNDSCQGDSGGPLVCGGRLRGLVSWGDMPCGSKEKPGVYTDVCTHIRW 243
            T+ MVCAG    G D+CQGDSGGPLVC G L+G+ +WG  PCG  EKPGVYT +C +  W
Sbjct: 193 TEGMVCAGS-SNGADTCQGDSGGPLVCNGVLQGITTWGSDPCGKPEKPGVYTKICRYTNW 251

Query: 244 IQNIL 248
            I+  +
Sbjct: 252 IKKTM 256
```

DEVELOPMENTAL DYNAMICS 208:553-564 (1997)

Trypsin-Induced Follicular Papilla Apoptosis Results in Delayed Hair Growth and Pigmentation

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ABSTRACT **Programmed cell death is a controlled process that leads to the elimination of single cells via apoptosis. Programmed cell death is fundamental to development, morphogenesis, and homeostasis. Proteases play a major role in the death process. We have previously shown that a serine protease, secreted by a keratinocyte cell line, can induce apoptosis in numerous cell lines. Here we show that serine proteases can induce cell death in vivo as well. Using a synchronized hair growth mouse model, we show that topical trypsin treatment following depilation induces cell death at the follicular papilla. This results in delaying hair growth and pigmentation. We speculate that trypsin might affect a receptor-mediated signaling pathway that leads to follicular papilla cell death. *Dev. Dyn. 208:553-564, 1997.***

Key words: apoptosis; hair cycle; hair follicle; trypsin; liposomes

INTRODUCTION

The hair follicle is an epithelial structure that undergoes cycles of active growth (anagen), regression (catagen), and rest (telogen) (Panaretto, 1993). The anagen phase involves the growth of the hair follicle down into the dermis, forming a complex layered structure with a pigmented shaft. Melanogenesis had been shown to be coupled to anagen (Slominski and Paus, 1993). During the catagen phase, the hair follicle shortens as its lower two thirds undergoes programmed cell death and apoptosis. In telogen the epithelial cells are resting and the hair shaft remains inside the short follicle until a new hair shaft is produced. Although the morphological changes throughout the hair cycle are well documented (Chase, 1954), only limited information on the molecular biology of that cycle has been described (see Panaretto, 1993; Stenn et al., 1994b, 1996; Seiberg et al., 1995).

The hair follicle is one of the few organs that cycle throughout adult life. This implies that a portion of the follicle must be permanent and responsive to the signal of cycle-reinitiation. Two regions of the follicle might fulfill these requirements (Cotsarelis et al., 1990; Reynolds and Jahoda, 1991a,b). One is the bulge area, an epithelial structure that contains a keratinocyte stem cell population that can generate a new follicle (Cotsarelis et al., 1990; Sun et al., 1991; Lavker et al., 1993). The other is the follicular (dermal) papilla, a mesenchymal structure that interacts with epithelial cells to induce hair growth (Reynolds and Jahoda, 1991b; Oliver, 1966; Jahoda et al., 1984; Oliver and Jahoda, 1988; Jahoda, 1992; Messenger, 1993). The follicular papilla dictates the nature of the follicle, and it can induce hair growth even from epithelia that are not normally associated with hair formation (Reynolds and Jahoda, 1990, 1991b; Jahoda, 1992). In order for the follicle to cycle, it is assumed that the bulge and the papilla must be protected from cell death. We have previously shown that *bcl-2*, a survival gene that rescues cells from programmed cell death, is expressed in the bulge region during anagen, and in the follicular papilla throughout the hair cycle (Stenn et al., 1994a).

Programmed cell death (PCD) is a fundamental aspect of development, morphogenesis, and tissue homeostasis. Many PCD pathways lead to apoptosis, a mode of cell death involving cytoplasmic condensation and specific DNA fragmentation (reviewed in Cohen, 1993; Fesus, 1993; Barr and Tomei, 1994; Martin et al., 1994; Bellamy et al., 1995; Kroemer et al., 1995; Vaux and Strasser, 1996). The controls and signals initiating cell death are only partially shared between different biological systems, but a common final pathway seems to be shared by all apoptotic pathways.

Cytoplasmic proteases play a functional role in PCD. The *Caenorhabditis elegans* protein *Ced-3* is essential for cell death and its mammalian-homologue cysteine proteases act as vertebrate PCD genes. Cell granule proteases (granzymes) induce apoptosis in permeabilized cells. Viral proteins that inhibit apoptosis have protease inhibitor activity. Experimental inhibition of cysteine or serine proteases inhibits apoptotic cell death in many in vitro systems (reviewed in Patel et al., 1996).

We have previously shown that a serine protease, secreted by the keratinocyte cell line Pam212, can induce apoptosis in numerous cell lines. Moreover, the induction of apoptosis in vitro was reproducible using trypsin (Marthinuss et al., 1995b). Here we show that serine proteases were able to induce apoptosis in vivo as well. Using a synchronized hair growth mouse model we show that a topical trypsin treatment immediately following depilation induces apoptosis in the follicular papillae. Cell death within the papillae results in a delay in hair growth and pigmentation.

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Received 21 August 1996; Accepted 14 January 1997

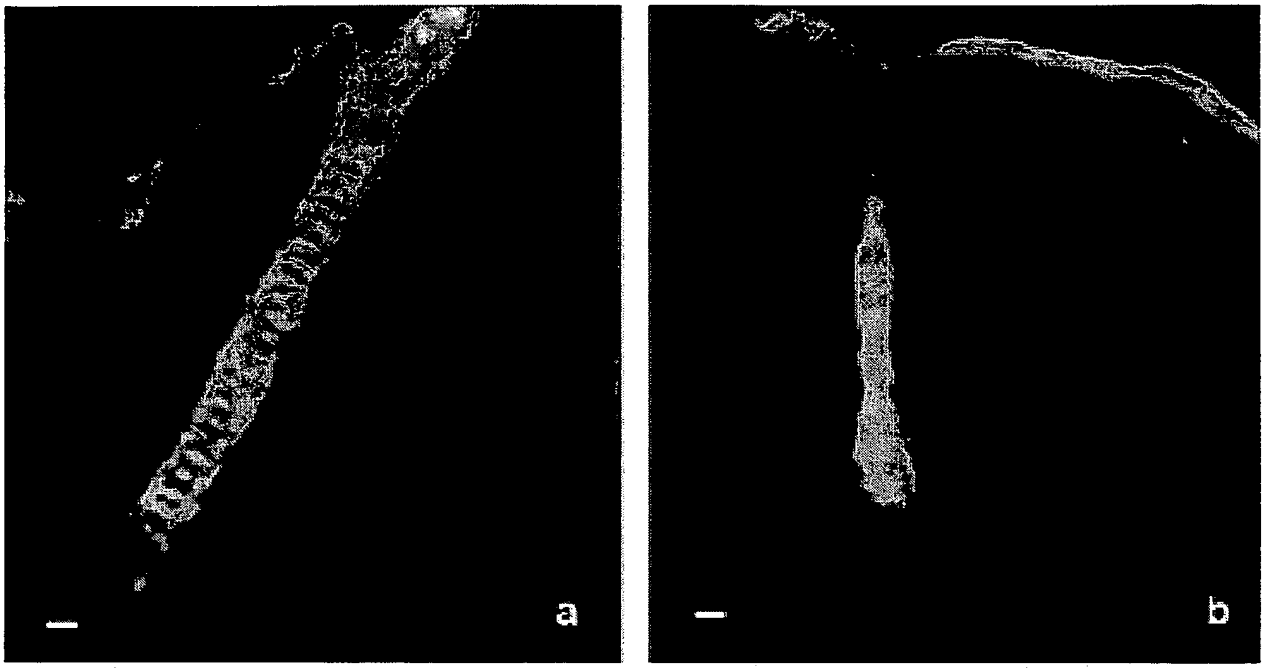

Fig. 1. Trypsin delivery into hair follicles. Untreated (**a**) and 12-day trypsin-treated mice (**b**) were painted with fluorescently labeled trypsin. Animals were sacrificed after 4 hr, and skins were processed for frozen sections. Bars = 10 μm.

RESULTS

Synchronization of Hair Growth in C57Bl/6 Mice

To determine whether serine proteases could induce apoptosis in vivo, we examined the effect of Trypsin on the mouse hair cycle. C57Bl/6 mice, at 6–10 weeks of age, are in the telogen phase of the hair cycle. Hair growth is induced by wax depilation (plucking) of the animal's back fur (Stenn et al., 1993). The growth phase (anagen) starts synchronously in all hair follicles at the time of depilation. The first histological changes are observed after one day (early anagen), when a new follicle starts to grow out from the bulge area. Several days after depilation, the hair growth is visible as the pink skin of the animal starts darkening. This is due to pigmentation in the shaft, as the C57Bl/6 mouse contains melanocytes only in their follicles and not in the epidermis (Slominski and Paus, 1993). By 3–4 days the hair follicle is fully developed, but the hair shaft is not yet visible. By 8 days (late anagen) the mouse has a very dark skin, and the hair shafts start to penetrate through the epidermis at days 11–12. At day 14 the mouse back is covered with short hairs. By days 19–21 the regression of the follicle (catagen) is observed histologically, and by days 21–25 the hair follicle is back to resting phase. A similar synchronized hair cycle could also be induced by chemical depilation. In that case, the lower portion of the follicle remains intact. Hair shafts of the previous cycle remain intact in the

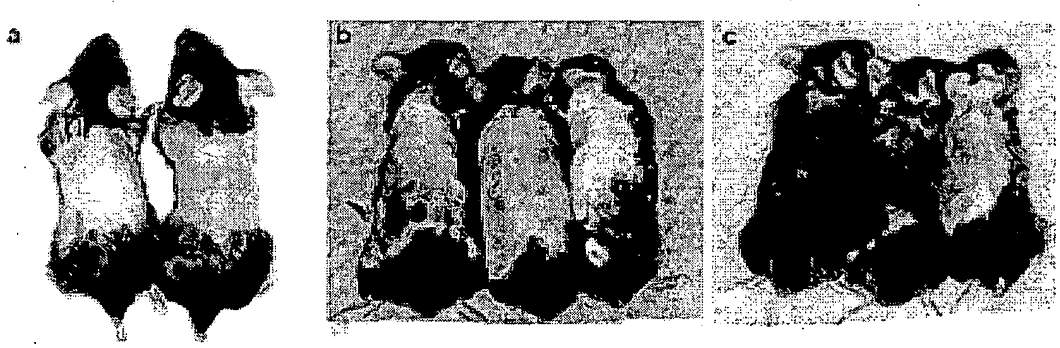

Fig. 2. Trypsin delays hair growth and pigmentation. C57Bl/6 mice were depilated and treated with vehicle or trypsin (1%) immediately after depilation. (**a**) 8 days post depilation. Left is treated, right is untreated. (**b**) 11 days and (**c**) 14 days post depilation. Left is untreated, middle is vehicle, and right is trypsin treated. Darker skin color indicates a more progressive stage of the hair cycle, before hair shafts are visible.

dermis, until pushed out by the new hairs. It is important to note that the murine hair cycle varies not only between strains, but also among individual animals. Therefore, each skin sample was examined histologically, to verify the phase of the hair cycle.

Delivery of Serine Proteases Into Hair Follicles

To examine the effect of trypsin on the hair cycle of the mouse, we needed to deliver serine proteases, 20–40 kD in size, into the hair follicles. The potential for the use of non-ionic liposomes to target the pilosebaceous unit has been previously demonstrated (Niemiec et al., 1995; Lauer et al., 1996). Using that delivery system, we were able to target proteases into the mouse hair follicles. The specificity of the delivery system was tested with fluorescently labeled trypsin using anagen animals (most stringent condition). Mice were topically treated with the labeled trypsin, sacrificed at 1 and 4 hr after treatment, and their skin was analyzed histologically.

As shown in Figure 1a almost all of the fluorescent labeling was found within the hair follicle. The 1-hr (not shown) and 4-hr (Fig. 1a) treatments with the tagged trypsin displayed an identical staining pattern, with no apparent additional skin penetration at the later time point. This observation rules out a possible non-specific skin extracellular matrix digestion by the protease (which would show as deeper penetration of the fluorescent stain into the stratum corneum at the later time point).

The effect of long-term trypsin treatment on the delivery system was also studied. Mice depilated (both chemically and by wax) and treated with trypsin daily for 12 days, were treated with the fluorescently labeled trypsin for 4 hr (Fig. 1b). No major change was observed in the delivery route into the hair follicles of the treated skin. A minimal staining at the outer portion of the stratum corneum of the trypsin-treated skins indicated some loss of barrier integrity. This was confirmed by measuring transepidermal water loss (TEWL, see Table 4 and Discussion).

In contrast to the non-ionic liposomes, using aqueous buffered solutions or lipid-based delivery vehicles (Granulex) was shown to be ineffective. We were unable to demonstrate the delivery of the protease into the hair follicle and observed no biological effects (not shown).

Trypsin Delays Hair Growth and Pigmentation

A single topical application of trypsin (1%) immediately after depilation had a dramatic effect on the hair cycle. As shown in Figure 2, both hair growth and pigmentation were delayed. Untreated controls exhibited dark skin at 7–8 days after hair growth induction, while trypsin-treated animals remained pink (not pigmented) until day 8 (Fig. 2a). The hair shafts of control and vehicle treated mice were visible at 11–13 days after depilation. At that time, the skin color of the trypsin-treated mice was darker, but still pink, and no hair shafts were visible (Fig. 2b). By 14 days, the control mice were covered with short fur, while trypsin-treated animals exhibited gray skin with no hair shafts (Fig. 2c). The hair shafts of the trypsin-treated mice were first visible at days 16–19. These hair shafts were of reduced quality (e.g., unequal shaft thickness), but within 4–7 more days, except for length, they were almost indistinguishable from the controls.

Histology of Trypsin-Treated Hair Follicles

Histological analysis of untreated, liposome control (identical to untreated, not shown) and trypsin-treated skins revealed major changes in the trypsin-treated animals. As shown in Figure 3, the hair follicles were delayed in their development. The characteristic layered structure, the expanded follicular papilla, and the new pigmentation were observed 5–7 days later than the controls, and the follicles displayed a dialated infundibulum (compare untreated follicles, Fig. 3A-a,b to trypsin-treated, Fig. 3B-a–e). At 7–8 days after treatment about half of the treated follicles started to overcome the trypsin effect and exhibited characteristic follicular development of a 3–4-day control follicle. The upper part of these follicles was still distorted, exhibiting a dialated infundibulum (See Fig. 3B-d). By 11–12 days most of the treated follicles matured, but still displayed reduced pigmentation and shorter shafts, resembling a 4–5-day control follicle (delay of 7 days, compare Fig. 3A-d to Fig. 3B-f). One fourth of the mature follicles remained histologically atypical (bends, kinks, unequal shaft thickness) throughout the observation period (14 days). The trypsin treatment results also in epidermal hyperplasia (see Fig. 3B), as it induces epidermal differentiation and increases the number of cell layers of the epidermis.

Trypsin Induces Apoptosis at the Follicular Papilla

Following wax depilation, we expected trypsin to induce apoptosis within the follicular papilla and around it, as the previous telogen follicle is removed. Upon chemical depilation we could affect the lower epithelial portion of the follicle as well. Terminal transferase end-labeling (TUNEL staining) revealed an increase in apoptotic figures in the trypsin-treated follicles, relative to untreated and vehicle-treated controls, regardless of the depilation system. As shown in Figure 4, apoptotic bodies were detected within the treated follicular papilla throughout the first week after hair growth induction (Fig. 4B-a–e). At a given time, only a few cells within a single papilla were affected. No other portions of the follicle, epidermis, or dermis were affected by the serine protease treatment. While a minimal level of apoptosis was occasionally detected in untreated early anagen follicles (see Fig. 4A-a–c), it was always at the isthmus of the follicle, well above the follicular papilla. Most of the untreated follicles did not display any cell death.

Continuous daily applications of trypsin also had a later effect on the growing follicle. At day 8 post

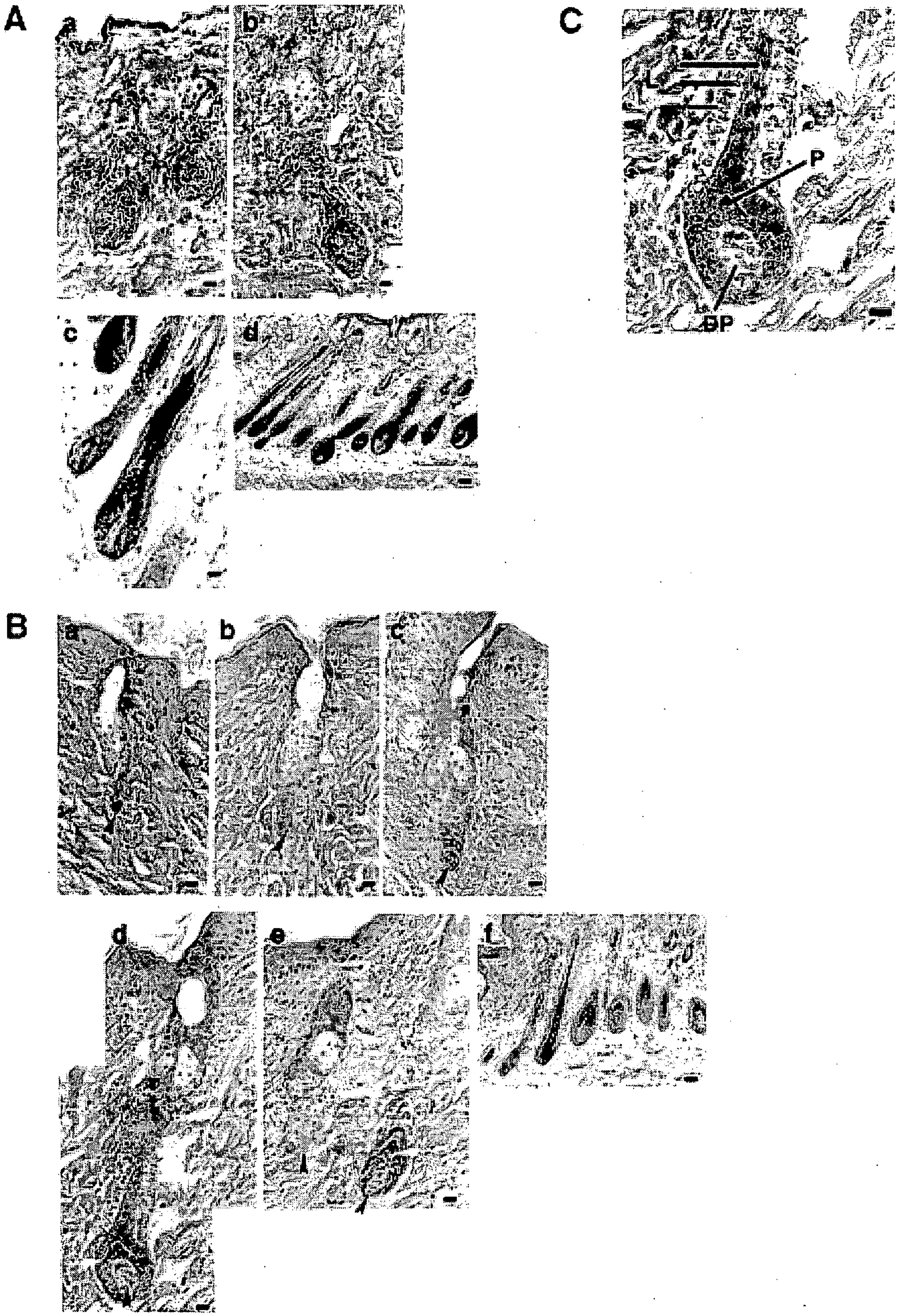

Fig. 3. Trypsin delays hair follicle development. Mice treated as indicated in Figure 2 were sacrificed daily and their skins were processed for histology using H&E staining. **A:** Untreated, days 4 (**a**), 5 (**b**), 8 (**c**), and 12 (**d**). Bar = 10 μm in a–c, 5 μm in d. **B:** Trypsin treated, days 4 (**a**), 5 (**b**), 6 (**c**), 8 (**d,e**), and 12 (**f**). Bar = 10 μm in a–e, 5 μm in f. Note that the follicular papilla of treated follicles (dark arrowhead) remains condensed up to 6 days post depilation (a–c). Layering structure and minimal shaft pigmentation (white arrowhead) appear in some, but not all follicles, only 8 days post depilation (d,e). **C:** Lower portion of a hair follicle, indicating the papilla (DP), the epithelial layering structure (L), and the developing pigmented shaft (P).

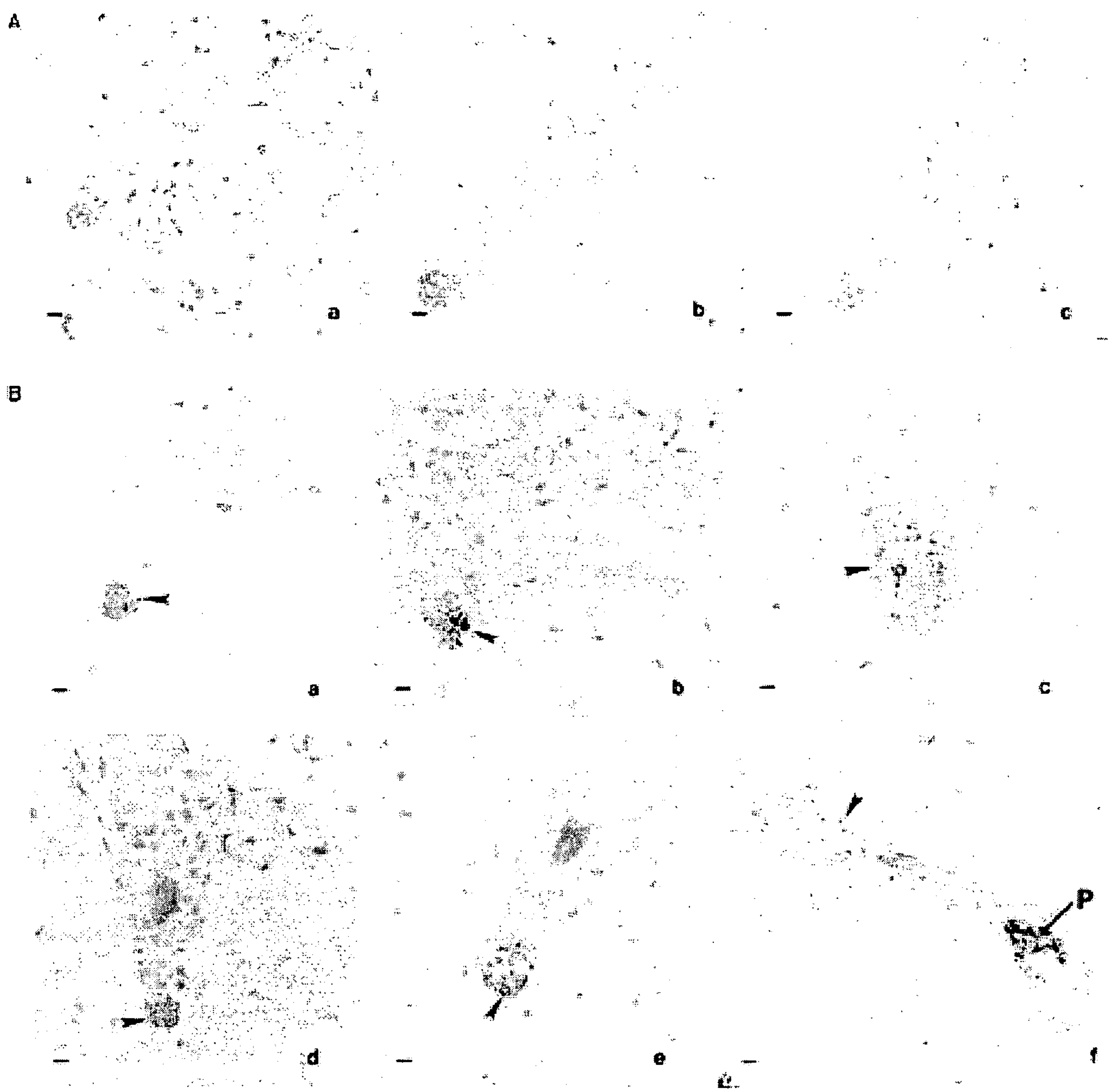

Fig. 4. Trypsin induces apoptosis in the follicular papillae. Mice were treated as indicated in Figure 2 and sacrificed daily. Paraffin sections were stained for apoptosis using a TUNEL stain with a peroxidase end point (brown), and methyl green counter-stain. **A:** Untreated, days 1 (**a**), 2 (**b**), and 3 (**c**) after depilation. Bar = 10 μm. **B:** Trypsin treated. **a–e,** 1–5 days after depilation, single trypsin application. **f,** daily treated for 8 days after depilation. Bar = 10 μm, in a,d,e and 5 μm in b,c,f. Apoptosis is detected only in the treated follicular papillae (arrowheads). Note the black pigmented shaft (P) forming above the follicular papilla, which is different from the brown TUNEL staining (f, see also pigment localization in Fig. 3).

depilation, about half of the daily treated follicles were able to overcome the protease effect and started to form layers (see Fig. 3B-d,e). These follicles exhibited minimal cell death at the upper follicular region, around the bulge area (Fig. 4B-f). Surprisingly, cell death at such an important region of the follicle had no effect on follicular development.

Trypsin Can Induce Changes in Gene Expression During the Hair Cycle

Several serine proteases have been recently implicated as mediators of signal transduction and regulators of gene expression (e.g., Patel et al., 1996). Our previous work suggests that serine protease(s) induce apoptosis in cultured cells via a signal transduction

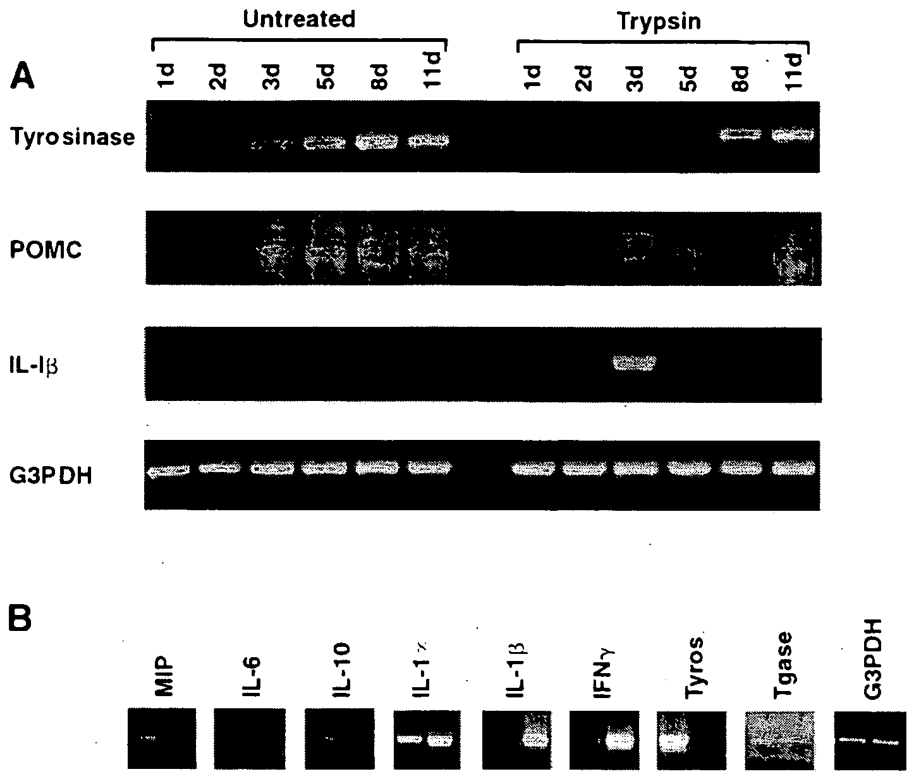

Fig. 5. Gene expression during the delayed hair cycle. Mice were treated as indicated in Figure 2 and sacrificed daily for RNA extraction. RT-PCR was used to compare steady-state mRNA levels of the genes indicated. **A:** mRNA levels (the RT-PCR product of 25 ng total RNA) throughout the delayed hair cycle. **B:** mRNA levels (the RT-PCR product of 250 ng total RNA, 5 ng for G3PDH) at day 8 of the cycle. For each gene tested in panel B, left is untreated, right is trypsin treated. (See also Table 1.)

mechanism (Marthinuss et al., 1995a,b), and we had shown changes in gene expression following serine protease treatment of cultured cells. Therefore, we examined the pattern of expression of a series of genes, throughout the hair growth-delay period. We chose the RT-PCR amplification assay for its sensitivity, even though it is semi-quantitative only. We clearly demonstrate trypsin-induced changes in mRNA levels along the hair cycle using this assay.

A strong increase was demonstrated for IL-1β and IFNγ mRNAs (Fig. 5A,B, Table 1), genes which are upregulated in Alopecia Areata and are associated with the inhibition of hair growth. A moderate upregulation was observed in IL-1α mRNA level (Fig. 5B, Table 1), a gene associated with the inhibition of hair growth in culture. Since IL-1α induction could also result from the loss of the epidermal barrier function, we analyzed the barrier integrity by measuring TEWL. A moderate increase in TEWL, which did not correlate with trypsin concentration, was always observed (see Table 4).

To verify that the delay in follicular development was not the result of a non-specific irritation or an inflammatory response, we analyzed the mRNA levels of genes that are upregulated during such situations. We found no change in the mRNA levels of IL-6, IL-10, and GM-CSF, a slight upregulation of TNFα, a slight downregulation of TNFβ and TNF-RI, and a moderate

TABLE 1. Patterns of Gene Expression at Day 8 Post Depilation[a]

Gene	Untreated	Trypsin
IL-6	−	−
IL-10	±	±
GM-CSF	−	−
TNFα	±	+
TNFβ	+	±
TNF-RI	±	+/−−
TNF-RII	−	−
MIP	+	−
IL-1α	+	++
IL-1β	±	+++
IL-1R	−	−
IFNγ	−	+++
c-myc	+	−
c-myb	++	+
c-fos	+	±
c-jun	±	+
Collagenase	+	±
Tyrosinase	+++	±
POMC	+	±
Transglutaminase	+	+

[a]For experimental details see Figure 5. Note that RT-PCR is semi-quantitative only. Comparisons are valid only for each amplified sequence, within the different hair cycles, and not among the different genes. −, no detectable expression; +/−−, a very weak band; ±, a weak band; +, a strong band; ++, a stronger band; +++, a very strong band.

downregulation in macrophage inducible protein (MIP). This profile of gene expression (see Fig. 5B, Table 1) rules out an inflammatory reaction or a response to dermal irritation. Moreover, mice treated with known irritants like hexadecane or SDS (1%), either at a single dose or using daily applications for 2 weeks, showed no effect on hair growth or pigmentation (not shown). Their gene expression profile was very similar to an irritation-induced gene expression profile (Kondo et al., 1994).

A slight reduction was detected in the mRNA levels of *c-myb, c-myc,* and *c-fos,* while the *c-jun* level was slightly increased throughout the delay period (see Table 1). Collagenase, a gene regulated via an AP-1 response element, was slightly reduced as well.

Tyrosinase, a key enzyme for hair pigmentation, was downregulated during the delay in hair growth period. Its mRNA level increased as the follicles start to overcome the delay (Fig. 5A). Proopiomelanocortin (POMC), the precursor of the melanogenic peptide melanocyte stimulating hormone (MSH), was moderately downregulated throughout the delay period (Fig. 5A). This indicates that trypsin could, directly or indirectly, affect the regulation of melanogenesis as well.

Transglutaminase, a gene induced in apoptosis and during catagen, did not exhibit a change in mRNA level during the delayed hair cycle (Fig. 5A, Table 1). This reflects the limited number of cells within the skin that are induced to death. At a given time, only a few of the papilla cells are affected by the protease death signal (see Fig. 4B). Changes in gene expression within such a small fraction of the skin could not be detected in a whole skin assay.

Correlations of gene expression patterns with the hair cycle should not be confused with expression within the hair follicle itself, since many cell types within skin could contribute to a cycle-dependent expression pattern. Some gene expression in total skin is hair cycle dependent. This includes changes in expression both within the changing follicle and within the skin itself (see Seiberg et al., 1995, and references therein).

Other Serine Proteases Have a Reduced Delaying Effect on Hair Growth

Our delivery studies (Fig. 1) indicate that the effect of trypsin on hair growth and pigmentation is not the result of non-specific proteolytic digestion within skin. To further address this question, the effect of several serine proteases on the mouse hair growth was analyzed. Chromameter measurements were used to compared skin color of mice, as skin darkness results from follicular development (Slominski and Paus, 1993). Mice treated with different serine proteases were analyzed for this pigmentation effect at 8 days post depilation.

Both Carboxypeptidase-Y (hydrolyses L-amino acids at the C-termini of proteins) and a nonspecific endopeptidase (Protease IV, cuts 56% of peptide bonds at neutral PH) had only a minimal delaying effect on hair growth. Subtilysin (nonspecific peptidase at alkaline PH), on the other hand, slightly increased the rate of hair growth. Trypsin (endopeptidase, cuts at the C-side of Arg, Lys), in comparison, induced the longest delay in hair growth. Chromameter readings of skin color fully correlate with the delaying effect (Table 2). Trypsin-treated skins were less pigmented than the Carboxypeptidase-Y- or Protease IV–treated skins; untreated skins (natural development of pigmentation) were slightly brighter than the Subtilysin-treated skin. This clearly demonstrates that non-specific proteolytic digestion is not the major cause for the delayed growth.

TABLE 2. Chromameter Measurements of Serine Protease-Treated Skins[a]

Treatment	Sample size	L*
Untreated	6	49 ± 0.30
1% Trypsin	6	56.1 ± 0.81
1% Subtilysin	4	42.9 ± 2.87
1% Endo-pep	4	51.8 ± 0.11
1% Carboxy-Y	4	51.9 ± 0.47

[a]C57Bl/6 mice, 8 days post depilation, were analyzed for skin brightness (L* scale: 0 = black, 100 = white). Animals were treated with a single dose of protease immediately after depilation. Carboxy-Y, carboxypeptidase Y; Endo-pep, nonspecific endopeptidase.

Trypsin Affects an Early Step in Hair Growth Induction

Additional daily trypsin treatments did not prolong the delay in hair growth. Two, three, and seven treatments per week, up to 2 weeks, resulted in an identical hair growth profile, both morphologically and histologically, when compared to a single application (not shown). Even though the follicular delivery is not changed (see Fig. 1b), no further delay in the hair cycle is observed with the additional treatments.

To analyze the timing of the papilla sensitivity to the death signal, mice were treated with a single dose of trypsin at different time points. Mice treated immediately post depilation showed the longest delay in hair growth and pigmentation (see Table 3). Mice treated 2 and 4 hr after hair growth induction still exhibited a delayed hair cycle, but progressively shorter. Mice treated 6 hr after depilation or at later time points were not delayed for hair growth and were indistinguishable from untreated control. Skin color measurements (Table 3) demonstrated an increase in darkness (more pigment, less of the delay) that correlates with the increased time between depilation and trypsin application.

Trypsin Effect Might Involve a Receptor-Mediated Mechanism

Mice induced for hair growth were treated with reduced concentrations of trypsin, from 1% down to 0.01% (4×10^{-4}M–4×10^{-6}M), and analyzed morphologically and colorimetrically for the dose effect on hair growth. Reducing the trypsin concentration prolonged

TABLE 3. Chromameter Measurements of Trypsin-Treated Skin[a]

Treatment	Sample size	L*
Untreated	6	49 ± 0.32
At depilation	6	56.1 ± 1.54
After 2 hr	4	54.4 ± 1.30
After 4 hr	4	53.3 ± 1.23
After 6 hr	4	48.0 ± 2.01
After 18 hr	4	49.2 ± 1.07
After 48 hr	4	50.4 ± 1.01

[a]C57Bl/6 mice, 8 days post depilation, were analyzed for skin brightness (L* scale: 0 = black, 100 = white). Animals were treated with a single dose of trypsin (1%) immediately following depilation, or as indicated.

TABLE 4. Physical Properties of Trypsin-Treated Skins[a]

Treatment	Sample size	L*	TEWL
Untreated	6	45 ± 0.97	27.01 ± 3.8
Liposomes	4	45 ± 1.03	29.81 ± 2.9
0.01% Trypsin	4	48.6 ± 1.01	36.89 ± 4.6
0.1% Trypsin	4	49.5 ± 1.07	43.2 ± 5.2
0.5%	4	47.7 ± 0.3	34.53 ± 4.9
1% Trypsin	4	47.9 ± 0.08	37.5 ± 3.9
1% Trypsin—inactive	3	51.2 ± 0.17	33.99 ± 6.2

[a]C57Bl/6 mice, 9 days post depilation, were analyzed for skin brightness (L* scale: 0 = black, 100 = white) and transepidermal water loss (TEWL; increases when barrier function of the epidermis is disrupted). Animals were treated with a single dose of trypsin, immediately after depilation. Trypsin was inactivated by incubating at room temperature for 48 hr, in aqueous solution.

the delay in hair growth and pigmentation by 1–2 days. Chromameter measurements of the treated skins revealed an increase in brightness (L*, more white, less pigment) that correlates with the decrease in trypsin concentration (down to 0.01%) and with the increase in the delay of the hair cycle (Table 4). This could suggest a receptor-mediated mechanism including desensitization with higher doses.

A receptor-based mechanism could involve the occupancy of the receptor by a ligand, or receptor activation by a proteolytic cleavage. To further analyze the mechanism of the trypsin death signal we used an inactivated preparation of trypsin (1%, 48 hr at room temperature in aqueous solution). This preparation was enzymatically inactive, but was not completely denatured. Such a preparation further enhanced the delay in hair growth. Chromameter measurements of treated skins show that animals treated with the inactive trypsin had the highest L* score (Table 4). The inactive and native trypsin preparations induced similar histological changes, with an increased delay in hair growth for the inactive preparation (not shown). This clearly indicates that the proteolytic activity of trypsin does not play a role in the delay of hair growth. Boiled trypsin, which is inactive as well but is completely denatured, did not have any effect on the hair cycle, morphologically or histologically (not shown). This indicates that the 3-D structure of trypsin, and not its proteolytic activity, might be essential for the delaying effect.

DISCUSSION

Using a synchronized hair growth mouse model (Slominski and Paus, 1993; Stenn et al., 1993) we show that topical trypsin treatment, immediately after depilation, induces cell death at the follicular papilla. This death signal, which is independent of the proteolytic activity of the protease, results in delaying hair growth and pigmentation. We speculate that trypsin affects a receptor-mediated signaling pathway that leads to follicular papilla cell death.

We had previously shown that keratinocytes can undergo spontaneous apoptosis in vitro (Marthinuss et al., 1995a). We had further demonstrated that a serine protease, secreted by the keratinocyte cell line Pam212, can induce cell death of numerous cell lines (Marthinuss et al., 1995b). Using cycloheximide, we demonstrated that this serine protease activates the death mechanism via a signal transduction pathway (Marthinuss et al., 1995b). We excluded the proteolytic activation of the thrombin receptor, PAR-2 (a protease-activated receptor expressed in keratinocytes; Santulli et al., 1995) and urokinase plasminogen activator, as a part of the death signaling pathway (Marthinuss et al., 1995b).

Here we demonstrate that serine proteases could also induce apoptosis in vivo, and probably via a receptor-mediated mechanism. We clearly demonstrate that the proteolytic activity itself is not necessary to induce the cell death. Reducing the trypsin concentration results in an increase in the delaying activity, suggesting receptor desensitization with higher doses. Since boiled trypsin did not affect hair growth, we speculate that the 3-D structure of the molecule might be important for this process. The timing of the protease application is very critical. The follicular papilla is sensitive to the death signal only during the early steps of hair growth induction. Daily application of trypsin had no additive effect on the hair cycle.

One possible mechanism for serine protease-induced apoptosis is the perforin-granzyme mechanism, employed by cytotoxic lymphocytes. The combined effect of perforin, a pore-forming protein, and granzymes, a family of granule proteins that includes many serine proteases, leads to apoptosis and DNA fragmentation of target cells (reviewed in Patel et al., 1996). One might claim that wax depilation causes enough damage to the remaining cells to enable the entry of trypsin without additional perforin activity. However, the waxing damage is not unique to the follicular papilla, so one might expect the induction of apoptosis in dermal and epidermal cells as well. Moreover, depilatory creams induce hair growth of telogen mice without physically damaging the lower portion of the follicle or the follicular papillae. Trypsin could induce the same delay in hair growth in the wax and chemically depilated animals.

The epithelial-mesenchymal interactions which lead to skin appendage formation are well studied (Hardy, 1992; Jahoda, 1992), demonstrating the important role of the follicular papilla in hair formation. The follicular papilla could induce follicle formation from the epithelium of the palm, which is usually not associated with hair follicles (Reynolds and Jahoda, 1991b; Jahoda, 1992). The combination of follicular papilla fibroblasts with epithelial cells results in pigmentation and hair follicle formation in nude mice (see Prouty et al., 1996, and references therein). Inducing cell death at the follicular papilla has not yet been described. Here we show that the induction of apoptosis in the follicular papillae results in perturbation of the hair cycle, and in delaying hair growth and pigmentation.

During the hair cycle the papilla changes its size by the addition of extracellular matrix molecules. The number of cells within this structure remains constant throughout the hair cycle (Messenger et al., 1991). The trypsin-induced apoptosis might result in a decrease in the number of cells within the papilla. It is possible that the delay in hair growth equals the time needed to regenerate these missing papillae cells. Maybe only when a damaged papilla is recovered, then new hair formation can take place. It is possible, also, that atypical hair follicles rise from a papilla that is not completely recovered. Such a mechanism could further demonstrate the importance of this mesenchymal structure in hair follicle formation. We cannot exclude the possibility that amelanotic melanocytes or endothelial cells were induced to death by the protease. The distribution of the apoptotic bodies within the papilla, however, does not resemble the localization of follicular melanocytes or endothelial cells.

We had previously shown that the localization of Bcl-2 (a protein that negatively regulates apoptosis) within the hair follicle is hair cycle dependent (Stenn et al., 1994a). The papilla continues to express *bcl-2* throughout the cycle, as well as during telogen, while the bulge area, where follicular stem cells reside, expresses this protective protein only during the growth phase. This supports the notion that the follicular papilla is a long-lived structure, and that its function is continuously necessary. The induction of papilla cell death by the proteases, therefore, might reflect on a special property of the papilla at the time of hair growth induction, which makes it sensitive to the death signal. This timing could correlate with the reduced expression of one or several members of the Bcl-2 family. Alternatively, the protease signal could act downstream of the *bcl-2* protection check point, as was shown for epidermal keratinocytes apoptosis (Marthinuss et al., 1995b).

Nexin-1, a serine protease inhibitor, is expressed within intact skin at the late anagen papilla only (Yu et al., 1995). Nexin-1 provides a mechanistic control for serine proteases at and near the cell surface of fibroblasts (Wagner et al., 1989). Nexin-1 had been shown to rescue neuronal cells from apoptosis (Houenou et al., 1995). It is conceivable that the expression of Nexin-1 enables the papillae to survive the protease death signal, possibly by complexing with the catalytic site serine residue and internalizing and degrading the complex. This would have the effect of changing putative follicular death into delayed growth.

Some gene expression within skin is hair cycle-dependent. We had demonstrated a change in patterns of gene expression immediately before and during catagen, which might be involved in the regulation, initiation, or execution of the regression of the lower follicle (Seiberg et al., 1995). The changes in gene expression induced by trypsin do not reproduce the pattern of gene expression during catagen. The general reduction in mRNA levels of several genes observed here is reflective of the overall slow down in hair growth, and not of catagen. This implies that the serine proteases do not induce premature catagen. Indeed, trypsin treatments during anagen did not induce the regression of the follicle. Moreover, while TNFα, EGF, and IL-1β can abrogate hair growth in organ culture, a catagen-like morphology is formed with TNFα and EGF, but not with IL-1β (Hoffmann et al., 1996). Here we show that IL-1β, but not TNFα, is highly upregulated by the serine protease induced papilla death, suggesting a mechanism different from premature catagen. Transglutaminase, a gene upregulated in apoptosis and catagen, is not upregulated by the trypsin signal. This also supports the notion that the death signal does not induce premature catagen. Changes in mRNA level of a few of the papilla cells cannot be detected by RT-PCR of total skin, while transglutaminase gene expression of regressing follicles is easily detected (Seiberg et al., 1995).

IL-1α and IL-1β are related proteins with broad biological activity, associated mainly with inflammation, but also expressed in non-immune cells including epidermal keratinoytes and fibroblasts. Both IL-1α and IL-1β can inhibit follicular growth in organ culture (Harmon and Nevins, 1993; Hoffmann et al., 1996), and transgenic mice overexpressing IL-1α in the skin exhibit patchy hair loss (Groves et al., 1995). In Alopecia Areata, when a cascade of immunological events results in hair loss, high levels of IL-1β expression has been reported (Hoffmann et al., 1994; Telegdy et al., 1994). We observe the highest increase in gene expression of the trypsin delayed hair cycle at the mRNA levels of IL-1β and IFNγ. The increase observed in IFNγ level also correlates with the IFNγ upregulation in Alopecia Areata (Hoffmann et al., 1994; Telegdy et al., 1994).

We demonstrate a significant increase in IL-1β mRNA, and a moderate upregulation in IL-1α mRNA level. While both could affect hair growth, it is important to note that IL-1α expression is also stimulated by epidermal barrier disruption (Wood et al., 1996). Our observation of increased TEWL indicates that the moderate increase in IL-1α could reflect the barrier effect, and might not be related to the hair growth delay. The increase in IL-1β during the delayed hair cycle might provide a clue to the mechanism of the perturbed

follicular growth. If IL-1β is involved in the maintenance of the delayed growth, then one might expect the follicle to remain dormant as long as IL-1β is expressed. This is, indeed, the situation in our study. When IL-1β levels start to decrease, the follicles start to overcome the inhibitory signal. This is observed histologically, and later also morphologically. At day 14, when the growth delay is over, the level of IL-1β mRNA is below detection. It would be interesting to analyze the levels of IL-1 receptor antagonist (IL-1ra) and melanocyte stimulating hormone (αMSH), two potent inhibitors of IL-1β, and find out whether an increase in one of these molecules downregulates IL-1β and abrogates the growth inhibition. These two regulators are expressed in skin: MSH has a major role in pigmentation (Wintzen et al., 1996), and IL-1ra gene polymorphism is associated with the severity of Alopecia Areata (Tarlow et al., 1994; Cork et al., 1995). IL-1 expression is high in undifferentiated keratinocytes, and is reduced when they become terminally differentiated (Ansel et al., 1988). Whether it is possible to draw an analogy to an undifferentiated (telogen) follicle vs. the growing, more differentiated (anagen) one, remains to be studied.

The increase in IL-1β and IFNγ could also reflect an inflammatory response or could result from epidermal irritation. To verify that the delay in follicular development is not the result of such non-specific processes, we analyzed the mRNA levels of several other genes that are upregulated during irritation and inflammatory situations (Kondo et al., 1994). The profile of gene expression demonstrated (see Table 1) rules out an inflammatory reaction or a response to dermal irritation. Moreover, animals treated with known irritants had no effect on hair growth and pigmentation. Their gene expression profile was very different, resembling the described irritant-induced gene expression profile (Kondo et al., 1994).

Tyrosinase, the major regulator of hair pigmentation (Sanchez-Ferrer et al., 1995; Mishima, 1994) was downregulated during the delay in hair growth period. Its mRNA level increased as the follicles started to overcome the delay (Fig. 5). Proopiomelanocortin (POMC), the precursor of several peptides including the melanogenic peptide MSH (Jimbow, 1995; Wintzen et al., 1996), was slightly downregulated throughout the delayed hair cycle. The cell death induced by the protease at the papilla, therefore, affects the pigmentation of the follicle. This implies that the follicular papilla has an important role in the regulation of melanogenesis as well.

In this study, we were able to manipulate the hair cycle via trypsin-induced apoptosis at the follicular papilla. This is the first demonstration of induced apoptosis in the follicular papilla, a structure thought to be protected from cell death. The proteolytic activity of the protease is not necessary for the death signal. We speculate that trypsin might affect a receptor-mediated signaling pathway that leads to follicular cell death. Whether trypsin blocks a survival signal or activates a death receptor remains to be studied.

MATERIALS AND METHODS

Chemicals

Serine proteases and other chemicals were from Sigma (St. Louis, MO). Granulex (Dow Hickam Pharmaceuticals Inc., Sugar Land, TX) contains 1.25% trypsin in Balsam Peru and Castor Oil. Trypsin was inactivated by either incubating at room temperature for 48 hr, or boiling for 10 min, in 0.05M Hepes PH 7.4. Proteolytic activity was analyzed by the PanVera kit (Madison, WI). Trypsin was labeled fluorescently using a Molecular Probes kit (Eugene, OR). GDL liposomes (50 mg lipids/ml) were prepared as described in Niemiec et al. (1995). The non-ionic liposomal formulation contains glycerol dilaurate/cholesterol/polyoxyethylene-10-stearyl ether ratio 58/15/27.

Animals and Hair Growth Induction

C57Bl/6 female mice, 7–8 weeks old, were purchased from Charles River (Kingston, NY). Hair growth was induced by wax depilation as previously described (Stenn et al., 1993), or by chemical depilation (Neat, Nair). Each experiment described was performed using both chemical and wax depilation, with similar results. A skin sample from each animal was examined histologically, using H&E stain. One hundred microliters of the protease solution were applied to the back of each animal. Each experiment was repeated at least four times, with at least three animals per group. Transepidermal water loss (TEWL) was measured with an Evaporimeter using standard techniques (Evaporimeter EPI, Servomed AB, Stockholm, Sweden). Color measurements were performed using the Minolta Chromameter model CR300 using standard techniques (Osaka, Japan).

TUNEL Assay

Apoptotic staining was performed on paraffin sections using Apoptag (Oncor, Gaithersburg, MD, manufacturer's protocol), a technique based on the labeling of fragmented-DNA ends (Gavrieli et al., 1992). Each experiment was repeated at least three times. Pictures presented are of a single experiment. Apoptotic cells were defined by both morphology (condensed or fragmented nuclei and cytoplasm or apoptotic bodies), and staining (fragmented DNA within the condensed nuclei or apoptotic bodies).

RT-PCR

At the time points indicated animals were sacrificed and total RNAs were extracted from whole skins (RNA Stat-60, Tel-Test B, Friendswood, TX, manufacturer's protocol). At least 3 animals were used for each time point studied, and samples were analyzed individually. Total skin DNased-RNA (200 ng) (Promega, Madison, WI, RQ1 RNase-free DNase, manufacturer's protocol) from each sample was reverse transcribed (Gibco-BRL,

Gaithersburg, MD, Superscript II reverse transcriptase, manufacturer's protocol), using random hexamers (Gibco-BRL). RT products were PCR-amplified (Taq polymerase, Perkin-Elmer-Cetus, Branchburg, NJ), using Clontech primers, Clontech positive control and Clontech PCR protocol (Clontech, Palo Alto, CA) for mouse glyceraldehyde-3-phosphate-dehydrogenase (G3PDH), transcription factors and cytokines. Transglutaminase primers were: sense: 5'AACCCCAAGTTCCTGAAG and antisense: 5'TTTGTGCTGGGCCACTTC. The reaction contained 2.5 mM $MgCl_2$ and the cycle was of 1 min at 94°C, 2 min 55°C, and 3 min at 72°C, for 35 cycles. Tyrosinase primers were: sense: 5'TCAGCCCAGCATCCTTCTTC and antisense: 5'CAGCCATTGTTCAAAAATACTGTCC. The reaction contained 5 mM $MgCl_2$ and the cycle was of 1 min at 94°C, 2 min at 45°C, and 3 min at 72°C, for 35 cycles. POMC primers were: sense: 5'AAAAGAAGAGAGAAGAGCGAC and antisense: 5'AGAGCTGAGACACCCTTACC. The reaction contained 2.5 mM $MgCl_2$ and the cycle was of 1 min at 94°C, 2 min at 55°C, and 3 min at 72°C, for 35 cycles. Collagenase primers were: sense: 5'AAGACCCCAACCCTAAGCAC and antisense: 5'CAGCACTGACGGTTTTCACC. The reaction contained 2.5 mM $MgCl_2$ and the cycle was of 1 min at 94°C, 2 min at 53°C, and 3 min at 72°C, for 35 cycles. PCR products were ethanol precipitated when required. For G3PDH, only 10% of the PCR reaction was used. PCR products were analyzed on 2% agarose/ethidium bromide gels. An RNA sample that was not reverse-transcribed was used as a negative control for each PCR amplification. Obtaining no band indicates the lack of genomic DNA contaminants. A six-month-old mouse skin (non-synchronized hair cycle) RT was used as a positive control when plasmids were not available. The migration of the RT-PCR products on the gels was always identical to the positive controls, and to the reported amplimer sizes. To compare the relative quality of the RT-PCR reactions, the transcription level of G3PDH, a "housekeeping" gene, was used as a control. G3PDH gene expression was found to be similar at all the time points examined (see Fig. 5), enabling analysis of the relative levels of gene expression for the desired genes.

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